JUNE, 1951

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

Surgery in Massive Hemorrhage of the Upper Gastrointestinal Tract

Treatment of Nonspecific Ulcerative Colitis with Aureomycin

Management of Hemorrhage from the Upper Gastrointestinal Tract

●

Sixteenth Annual Convention
Chicago, Ill., 17, 18, 19 September 1951

VOLUME 18 NUMBER 6

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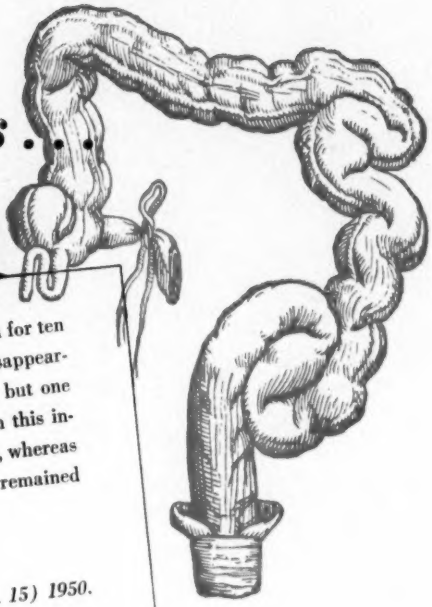

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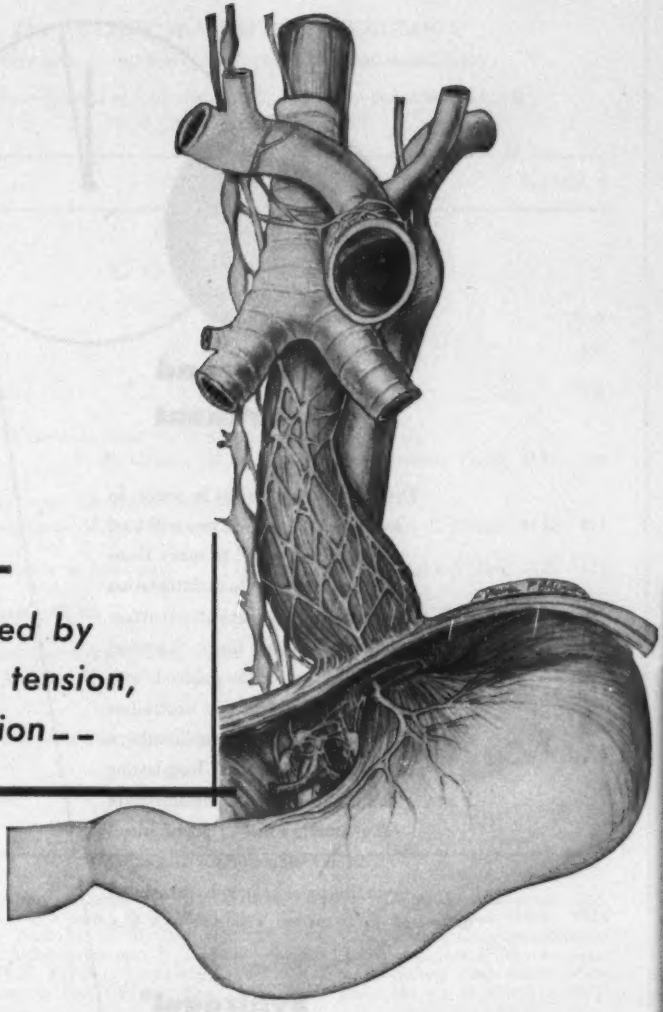

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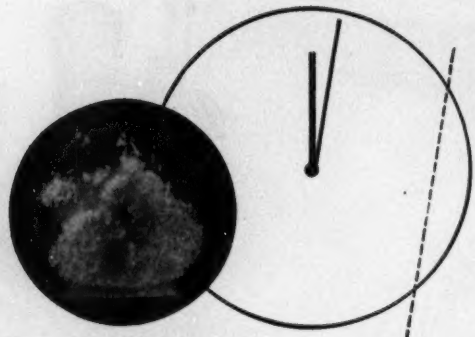

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(INCORPORATING THE AMERICAN JOURNAL OF GASTROENTEROLOGY)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

VOLUME 18 JUNE, 1951 NUMBER 6

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of the

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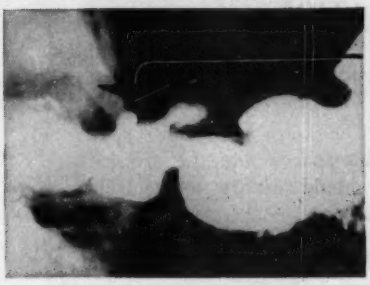
in peptic ulcer



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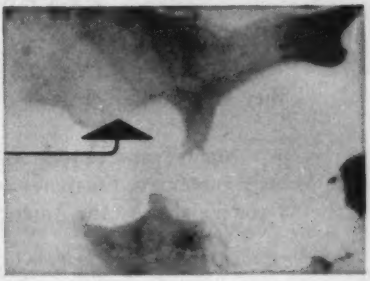

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*Offenkrantz, W. G.: Rev. Gastroenterol, *17*:359, 1950.

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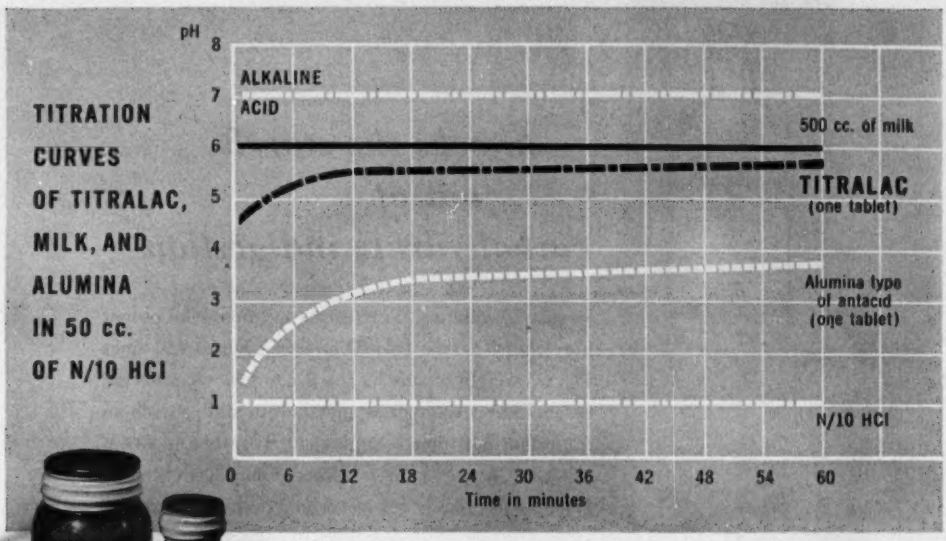

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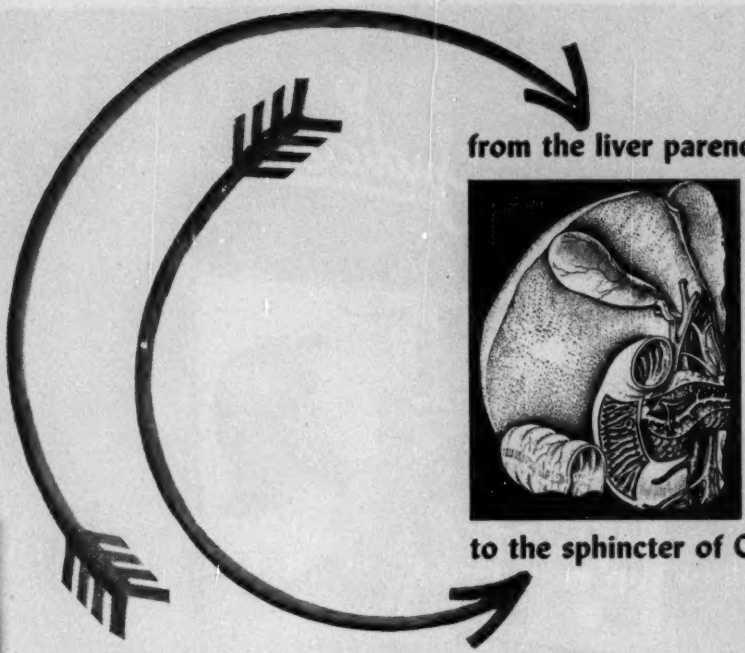

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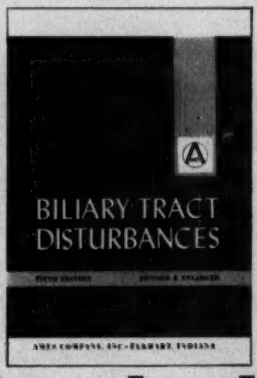

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The Review of Gastroenterology

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Volume 18 JUNE, 1951 Number 6

MANAGEMENT OF HEMORRHAGE FROM THE UPPER GASTROINTESTINAL TRACT*

N. W. CHAIKIN, M.D., F.A.C.P.†

and

THEODORE TULLER, M.D.‡

New York, N. Y.

Hemorrhage from the upper gastrointestinal tract frequently presents difficult problems, both from a diagnostic and a therapeutic point of view. This applies particularly to patients who are seen for the first time. In order to evaluate our clinical data with respect to etiology and therapeutics, we have reviewed 260 cases treated on the wards of Flower and Fifth Avenue and Metropolitan Hospitals. Only cases which presented gross hematemesis and melena were included.

Etiology

One hundred and ten cases were due to peptic ulcer, 71 of unknown etiology, 55 due to cirrhosis of the liver, 6 due to hypertension, 10 due to carcinoma of the stomach, 3 due to lymphosarcoma of the stomach, 3 due to carcinoma of the esophagus, and 2 due to erosions of the stomach.

Peptic Ulcer

The incidence of bleeding in peptic ulcer patients has been reported by investigators as varying from 10 to 38 per cent. Turnbull and Sagi[1] reported an incidence of 16 per cent; Hurst and Ryle[2], 31.3 per cent; Blackford and Cole[3], 19 per cent; Goldman[4], 38 per cent; Chaikin and Tannenbaum[5], 13 per cent. In our own series of 267 cases of peptic ulcer, which includes 136 cases previously reported and 21 cases from the unknown group which proved to be peptic ulcer, an incidence of 14 per cent was found.

---

*Read before the Fifteenth Annual Convention of the National Gastroenterological Association, New York, N. Y., 9, 10, 11 October 1950.

†Assistant Professor, Clinical Medicine, New York Medical College, Flower and Fifth Avenue Hospitals; Attending Physician, Metropolitan Hospital; Chief of Gastroenterological Clinics of Flower and Fifth Avenue and Metropolitan Hospitals; Assistant Attending Physician, Flower and Fifth Avenue Hospitals.

‡Assistant Physician, Metropolitan Hospital.

Age Incidence

Hemorrhage as a complication in peptic ulcer may occur at any age. The youngest in our group was 15 and the oldest 77, with the highest incidence between the ages of 40 and 50.

TABLE I

Ages	15-20	21-30	31-40	41-50	51-60	61-70	71-80	Total
Cases	39	53	65	85	18	5	2	267

The incidence given corresponds closely to the age incidence given by Jankelson and Segal[6], LaDue[7], and Crohn and Lerner[8].

In relation to sex, hemorrhage occurred in the ratio of 9.5 males to 1 female in the entire group. Distribution of the type of ulcer was as follows: duodenal ulcer 228; gastric ulcer 33; marginal ulcer 2; combined gastric and duodenal ulcer 4.

Factors Predisposing to Hemorrhage in Peptic Ulcer

1. Dietary Indiscretions:—Patients who adhere to a dietetic regime and who are under close medical observation, do not bleed. This is readily seen in the statistical disproportion between hospital referred cases and those treated in the outpatient department of the gastrointestinal clinic. The incidence of hemorrhage in hospital referred cases was 14 per cent while in those referred from the outpatient department for the same complication, it was slightly more than 1 per cent (3 in 285 cases)[9]. A great number of these patients from the outpatient department are publicly supported and given additional financial assistance for special diets. Their return to the clinic at specified intervals is necessary in order to maintain their financial aid. This almost compulsory attendance results in close observation of the patient at frequent intervals with subsequent decrease in the complication of hemorrhage. In like manner, the incidence of hemorrhage in office patients is directly related to the degree of adherence to the dietetic regime.

2. Respiratory Infections:—The relationship of recurrence of ulcer symptoms to respiratory infections has been observed by many clinicians. In a number of our patients, hemorrhage occurred in 10 days to 2 weeks following upper respiratory infection. Whether these respiratory infections are associated with acute erosions or acute ulcers or actual recurrence of a peptic ulcer is difficult to say. While there is no actual proof that focal infections play any part in the pathogenesis of chronic peptic ulcer, the frequent relationship between respiratory infections and recurrences, especially associated with hemorrhage, assumes a great practical importance. In ulcer-bearing patients, strict adherence to ulcer regime during respiratory infections should be stressed.

3. Trauma:—Trauma as a cause in initiating hemorrhage in peptic ulcer patients has taken on a new aspect in recent years because of its relationship to the Workmen's Compensation Laws. In the presence of an ulcerating lesion, a blow to the abdomen may traumatize the wall of the viscus and thus cause a hemorrhage. Where heavy lifting is followed by hemorrhage, the probable

mechanism is that of elevation of the arterial and venous pressure, with rupture of a vessel within the ulcer. In 5 of our cases, trauma to the abdominal wall and lifting of a very heavy weight were the direct initiating causes for the bleeding, as well as for the exacerbation of symptoms in a previously silent ulcer. For example, a mechanic working in a garage was suddenly attacked and received a forcible blow to the abdomen. Within a short period of time the patient began to complain of abdominal pain and passage of black stools. Upon investigation, the patient was found to have a peptic ulcer. Another patient, who for several years was known to have had an inactive duodenal ulcer, lifted a very heavy weight and in about 8 hours noted the passage of a massive tarry stool. Following this, he had a reawakening of his ulcer syndrome. In a third instance, a patient who was free from any gastrointestinal symptoms, was in a violent explosion and immediately following the accident had typical symptoms of ulcer with profuse hematemesis and melena. Because of the profuse hemorrhage and inability to control it, surgical intervention was deemed necessary. Exploration revealed an acute bleeding duodenal ulcer without evidence of scarring around the area. The remaining 2 cases which were associated with blows to the abdomen were followed by ulcer symptoms with bleeding from 3 days to 2 weeks after the date of the injury.

4. Psychogenic Factors:—Psychic trauma and anxiety states preceding the hemorrhage are so frequently obtained from the history of patients with peptic ulcer, that their relationship to the onset of bleeding is more than coincidental. The actual production of an ulcer in a human as a result of psychogenic stimulation was observed by Wolf and Wolff[10]. Prolonged stimulation may result in penetration, which may include a blood vessel, with subsequent bleeding.

5. Alcohol:—A history of an alcoholic spree followed by profuse hemorrhage has been elicited from a number of patients. The mechanism is by direct irritation of the ulcer and by stimulation of excessive gastric secretion.

6. Finally, in 25 per cent of the cases, no predisposing cause could account for initiating the hemorrhage; neither was the patient aware of the presence of an ulcer.

Idiopathic Group

There is a group of cases of hemorrhage from the upper gastrointestinal tract which defies any classification as to the origin of the bleeding. Among the 260, 71 such cases were encountered which failed to reveal any evidence of lesions 2 to 3 weeks following the hemorrhage. Negative radiological findings are a common occurrence following bleeding. Hemorrhage encourages healing of the ulcer with elimination of the filling defect. Crohn et al.[8] had observed 7 cases in which resection of the stomach and duodenum was performed a few weeks after hemorrhage from duodenal ulcer. The ulcer, in all instances, was found in a far advanced stage of healing. Twenty-one of these 71 cases finally proved to be peptic ulcer following repeated radiological examinations over a period of 6 to 12 months. Eighteen of the remaining 50 were followed-up for a period of 4 years. Three of these 18 finally proved to be due to hepatic cirrhosis. At the time of the hemorrhage, there was neither clinical nor laboratory evidence of liver disease.

These cases represent a latent cirrhosis, and the bleeding is due to a compensatory dilatation and stasis in the esophageal veins before other signs of portal hypertension manifest themselves. Four were subjected to subtotal gastrectomy because of recurrent hemorrhages and no demonstrable cause for bleeding could be ascertained at the time of the operation. In the remaining 11, hemorrhages recurred during the 4-year period, none of which were fatal. Gastroscopy in 7 showed a superficial gastritis.

Cases of idiopathic bleeding from the upper alimentary tract have been observed by a number of investigators. Jankelson[11] found 9 per cent of 685 cases of unexplained hemorrhage even though, at operation, the stomach and duodenum were opened up and examined from within. Eads[12] has reported 6.9 per cent of 129 cases of hemorrhage as undiagnosed. Schiff[13] was unable to classify 26.4 per cent of his cases of hemorrhage. Stone[14], in a review of 72 cases, was impressed by the great number of cases in which the cause for hemorrhage could not be explained in spite of the one or more laparotomies performed. Whether bleeding in these cases is due to hypertrophic gastritis, as expressed by Benedict[15], is open to further investigation. One pertinent fact stands out. Where no organic lesions could be demonstrated, the hemorrhages were rarely fatal.

Hypertensive Group

Hemorrhage occurred in 6 patients with known hypertension, the blood pressure varying from 220/130 to 190/100. None of these gave any history of preceding gastric disturbances. Radiological examinations were negative on repeated examination and gastroscopy performed in 2 patients failed to reveal the source of bleeding. In one patient, the blood pressure dropped from 220/130 to 130/90 and so remained for 8 months. In another patient, the pressure dropped from 190/100 to 140/80 and returned to its previous level within 6 days. A third patient died of myocardial infarction 14 months following hemorrhage and a fourth sustained a vascular accident. The gastric vessels are very infrequently implicated in arteriosclerosis. Very few cases have been reported in the literature where advanced arteriosclerosis of the gastric arteries has given rise to pathological lesions in the stomach. Gallard[16] reported 2 cases of fatal gastric hemorrhage which, on postmortem, revealed small mucosal erosions with aneurysmal dilatations of the small arteries at their bases, which he interpreted as due to arteriosclerosis. Sachs[17] reported a fatal case of gastric hemorrhage in a 79-year-old male, with an exposed miliary aneurysm of a small submucosal vessel, which he considered to be arteriosclerotic. Markwald[18] described a case of recurrent hematemesis in a man with an arteriosclerotic right coronary artery of the stomach. William Frank[19] reported a case of gastric arteriosclerosis with repeated hematemesis.

The incidence of sclerosis of the submucosal gastric arteries was studied at The Mount Sinai Hospital, New York City, in 100 consecutive stomachs opened at postmortem and, in only 2 cases, aged 57 and 65, was unquestionable evidence of intimal thickening with eccentricity of the lumen found. In 35 instances, 11 of which were hypertensive, minimal to mild intimal thickening was seen. Whether

these mild changes are clinically significant is questionable. Where arteriosclerosis of the gastric arteries was a prominent feature, the clinical picture was that of unexplained repeated gastric hemorrhage occurring from adolescence to senescence, and in none of the cases was an antemortem diagnosis made. In the cases presented above, the etiological factors of the bleeding cannot be explained. One may mention the controversial subject of gastric ulcers due to the sclerosis of the gastric artery. While, as previously stated, arteriosclerosis of the gastric vessels is rather an uncommon occurrence, nevertheless, the fact that the age of the patients varied from 60 to 82, absence of demonstrable pathology and the presence of the common denominator of hypertension in all cases, would lead one to conclude that arteriosclerosis with rupture of a terminal, nutrient vessel or thrombosis with autodigestion may be responsible for the bleeding in this group of patients.

Carcinoma of the Stomach

Carcinoma of the stomach is not a common cause for hemorrhage. It occurred in 4 per cent of our cases. However, it should be emphasized that hemorrhage may be the initial symptom. This occurred in 3 of our cases. Two of the 3 were discharged with a diagnosis of gastric hemorrhage of unknown etiology and readmitted within 6 to 8 months for another bleeding episode with typical radiological findings of an ulcerating carcinoma. A third patient was admitted with profuse hemorrhage which proved to be fatal. At postmortem examination an ulcerating carcinoma of the posterior wall of the stomach was found. In the remaining 7, the diagnosis of carcinoma was made without any difficulty.

Erosions

Two patients were admitted for repeated hemorrhages. Radiological examinations were essentially negative. Gastroscopy, however, revealed small erosions throughout the entire mucosa.

Lymphosarcoma of the Stomach

Lymphosarcoma of the gastrointestinal tract is rather rare and especially primary lymphosarcoma of the stomach. The general ratio of lymphosarcoma to carcinoma of the stomach has been given as 1 to 88 by Spellberg and Zivin[20], and as 1 to 71 by Warren and Lulenski[21]. The diagnosis of lymphosarcoma of the stomach is determined with great difficulty; the radiological appearance is greatly diversified. Hemorrhage due to lymphosarcoma is not sufficiently stressed in the literature. In 3 of our cases, hematemesis was the presenting symptom. Two of the patients had a fundal lesion and one simulating a gastric ulcer.

Carcinoma of the Esophagus

Erosions of carcinoma of the esophagus into large vessels is rather uncommon. Three patients presenting themselves with hematemesis were found to have carcinoma of the esophagus. One of these came in with an exsanguinating hemorrhage which, at postmortem, proved to be due to erosion into the aorta.

Cirrhosis of the Liver

Fifty-five cases of hemorrhage admitted to the hospital proved to be due to cirrhosis. Portal hypertension has been generally accepted as the cause for hemor-

rhage in cirrhotics. The disturbance in the prothrombin mechanism is probably a cofactor in inciting or prolonging bleeding. In most of our cases, however, there was no evidence of prothrombin deficiency.

The Pathogenesis of Portal Hypertension and Esophageal Varices

The tributaries of the portal vein constitute the venous drainage from the gastrointestinal tract. A block of this venous return which may occur within the liver as in cirrhosis, or extrahepatically along all or part of the portal system, will result in portal hypertension, which subsequently leads to formation of esophageal varices. Communication between the portal and caval systems takes place by way of the esophageal veins. They have at one end anastomoses with the splenic and coronary veins of the portal system and at the other with the azygos, intercostal and diaphragmatic veins of the systemic circulation. The absence of valves in the coronary veins makes a reversal of direction of blood flow possible, so that in portal hypertension, the blood tends to dam back and enter the systemic circulation by way of the esophageal veins. The damming back of blood from the portal system through the coronary vein overtaxes the capacity of the esophageal veins and in this manner varicosities begin. Additional factors which contribute to their development are the poor support which the esophageal veins receive from the loose connective tissue of the esophageal submucosa and the sucking action of the diaphragm during respiration. The anatomic location of esophageal varices constantly exposes them to trauma which may lead to fatal bleeding.

The frequent finding of ruptured esophageal varices which has been variously estimated as between 25 and 80 per cent (Ratnoff and Patek[22], and Preble[23]), lends further emphasis to the primary factor of portal hypertension as the cause of bleeding in liver cirrhosis. It should be pointed out that fatal hemorrhages in cirrhosis are not always due to esophageal varicosities. Varices of the upper third of the stomach and hemorrhagic gastritis are not unusual findings. Of the 55 patients admitted, 20 died during their stay in the hospital which varied from 1 to 120 days. In 6, necropsy revealed no evidence of esophageal varices, 2 showed marked congestion and oozing from the entire mucosa of the stomach, 3 showed varices of the upper third of the stomach, and 1 failed to show any cause for bleeding. The immediate cause of hemorrhage from the esophageal varices is not always clear and not always the same. Any sudden increase in the obstruction to the return flow of the blood will cause rupture of a varix. In some cases, the hemorrhage follows paracentesis as it did in 2 of our patients where bleeding followed 5 and 7 days after paracentesis. In 3 cases, the hemorrhage preceded sudden extreme muscular exertion; and in 1, it followed a heavy meal. In most cases, however, the hemorrhages were spontaneous.

Biochemical Changes

Elevation of blood urea nitrogen was the most constant finding. The blood chlorides and acid-base equilibrium were usually normal. The degree of elevation of blood urea nitrogen ranged from 20 to 88 mg. per 100 c.c. The daily determina-

tion of blood urea nitrogen was a valuable aid in appraising the clinical course and the prognosis. Where bleeding had ceased, the blood urea nitrogen came down to normal levels within 3 to 4 days. Failure of the urea nitrogen to return to normal was indicative either of continued bleeding, exacerbation of the bleeding, or renal impairment. Hyperazotemia in these cases depends upon the alimentary absorption of digested blood protein (Christiansen[24], Ingegno[25], Clausen[26]). The blood urea is a direct expression of the amount of blood protein absorbed from the bowel. There are, however, cases of hematemesis and melena where the hyperazotemia is due to renal impairment rather than to the absorption of blood protein from the bowel. The highest values were found in patients with shock and prolonged bleeding. It is exceedingly important in these cases to maintain a daily urinary output between 1,000 and 1,500 c.c. Where the urinary output could not be maintained in spite of parenteral fluids, the prognosis was poor.

Treatment

Therapy depended upon the following criteria:

(1) presence or absence of shock.

(2) hematocrit levels.

(3) stabilization of blood volume.

(4) presence or absence of renal impairment.

(5) presence and duration of pain.

All cases were divided into four groups:

Group I:—Moderate hemorrhage. These patients showed no evidence of shock, and hematemesis and melena were the outstanding symptoms. Hematocrit readings were above 30 and blood loss about 500 c.c. Treatment essentially consisted of immediate and persistent small hourly feedings of a modified Meulengracht diet. Additional medication consisted of antispasmodics and sedation. Patients were carefully observed for further bleeding, frequent blood pressure readings were taken, daily determinations of blood urea and stool examinations for blood were done. In this group, 136 patients were treated. Only one mortality occurred. It is questionable that this could be attributed directly to hemorrhage since this patient had a perforation while hospitalized. It should be stressed that patients with gastrointestinal hemorrhage who show no evidence of clinical shock, should not be transfused and no intravenous fluids should be given. In patients with a normal blood volume, introduction of fluids may prolong the bleeding.

Group II:—Moderate hemorrhage with shock. Blood loss was moderate and blood volume was readily restored. One or 2 transfusions were sufficient to stabilize the circulation. Where the blood urea nitrogen was above 60 and the urinary output low, parenteral fluids were administered in addition to transfusions. After the emergency had passed, nutrition was instituted as previously outlined in Group I. Patients were further observed by frequent readings of blood pressure, daily blood urea nitrogen determinations, and stool examinations for blood. One hundred and fifteen patients were treated in this group. Two mortalities occurred,

neither due to direct exsanguination. One was due to myocardial infarction 4 days following the hemorrhage, and the other occurred while being transfused.

Group III:—Profuse hemorrhage with shock. These patients required a number of transfusions to restore their blood volume, some needing as many as 5 or 6 transfusions. They recovered from shock and responded well to transfusions and nutrition. However, they continued to bleed as evidenced by tarry stools, falling hematocrits, and failure of blood urea nitrogen to come down to normal levels. Out of 70 patients in this group, 9 died. One questions the rationale of medical therapy and one wonders about the number of patients who could be salvaged by surgical intervention. However, the failure to subject these patients to surgery was justified by (1) questionable diagnosis, (2) bleeding for days prior to admission, and (3) poor surgical risk. It would seem that where there is evidence of continuous bleeding, surgery should be the therapy of choice providing the patient is a good surgical risk.

Group IV:—Profuse hemorrhage with shock and persistent pain. This group failed to respond to continued transfusions. Clinically, they manifested persistent hypotension, repeated bouts of hematemesis, melena and constant pain. These patients were referred to surgery. It cannot be emphasized too strongly that patients with this clinical picture should be referred to surgery immediately as they show a high incidence of perforation.

Treatment of esophageal varices, which is the most dreaded complication in patients with portal hypertension, is very unsuccessful. These varices are frequently silent, asymptomatic and rupture suddenly. Diagnosis is difficult and frequently goes unrecognized until there are a few episodes of bleeding. The treatment is purely supportive, namely transfusions, sedation and dietary precautions. The injection of sclerosing solutions into the esophageal varices has been recommended, but poor visualization makes this a hazardous procedure. Since major surgical interventions in these exsanguinated patients is too risky, the use of an intraesophageal tamponade (as recommended by Rowntree[27]) can be a lifesaving device. Direct pressure is exerted upon the bleeding point by means of an inflated balloon attached to a double lumen tube. We used this procedure in 3 of our cases with excellent results.

However, none of these procedures is physiologically sound because they do not reduce the portal hypertension. The only physiologic approach is to reduce the pressure in the portal vein which will, in turn, decrease the pressure in the esophageal veins. A portacaval shunt is the procedure of choice, and it has been recently advocated by Blakemore, not only to eliminate the threat of a fatal hemorrhage, but also to relieve a concomitant ascites.

Discussion

It must be clearly understood that the therapeutic approach to the management of hemorrhage from the upper alimentary tract can neither be generalized, nor can one be too dogmatic about any specific program. Each case must be individually evaluated in order to obtain the best therapeutic results. It is generally accepted that certain patients will die no matter what regime is followed. One can, however,

be guided by results obtained from treating these cases over a period of years. Prompt and persistent feeding has definitely lowered our mortality rates. Prior to 1937, the therapy in our own institutions consisted mainly of starvation, immobilization, and use of morphine with an overall mortality rate of 6.9 per cent. In a fairly similar group of 251 patients, treated with immediate feedings, no mortality could be attributed directly to exsanguination. In a statistical survey of 2,111 cases reported by Rasberry and Grier[28], the gross death rate was 4 per cent for cases treated by a prompt feeding program, with 8.5 per cent mortality in 5,843 cases collected by Miller and Elsom[29], all of which were treated by the commonly accepted conservative methods.

The high mortality rate in the third group (9 out of 70) is rather difficult to evaluate. As previously stated, these patients bled for days prior to admission and were very poor surgical risks. The high mortality rate in this group would seem to suggest that in patients in whom the hemorrhage does not subside, surgery should be resorted to providing the patient is a good surgical risk.

Daily determination of blood urea nitrogen is of great value in appraising the extent and duration of the hemorrhage and presence of renal impairment. In 6 of the 9 cases in Group III who died, the blood urea nitrogen varied from 60 to 70 mg. per 100 c.c. and, at no time, had it returned to normal levels. Failure of the blood urea nitrogen to return to normal levels after 3 or 4 days is, by itself, a poor prognostic sign, as well as an indication that the hemorrhage has not subsided. Where shock was present and the blood urea nitrogen high with a low urinary output, renal impairment was present. In these cases, every attempt should be made to maintain a proper urinary output. Profuse hemorrhage associated with shock and persistent pain is frequently indicative of perforation and should be immediately subjected to surgery. The therapy of hemorrhage from ruptured esophageal varices is essentially supportive. Where conservative treatment fails, an intraesophageal tamponade can be a lifesaving device, subsequently to be followed by a portacaval shunt.

Summary and Conclusions

1. Two hundred and sixty cases of hemorrhage from the upper alimentary tract are reviewed in addition to 136 cases of bleeding from peptic ulcer previously reported.

2. All cases, exclusive of cirrhosis and neoplasms, were classified into four groups.

3. All cases except the fourth group were treated medically by immediate and persistent feedings, and with transfusions where shock was present.

4. There were 3 deaths (out of 251) not directly attributed to hemorrhage in the first and second groups; and 9 deaths (out of 70) in the third group directly due to exsanguination.

5. Patients who do not respond to therapy within a few days should be referred to surgery.

6. Where profuse hemorrhages are associated with persistent epigastric pain, immediate surgery is the therapy of choice.

7. In the idiopathic group, fatal hemorrhages are rare.

8. Daily determinations of blood urea nitrogen are a valuable adjunct in evaluating the clinical course and prognosis.

9. The treatment of bleeding from esophageal varices is purely supportive; an intraesophageal tamponade should be used where other methods fail, to be subsequently followed by a portacaval shunt.

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TREATMENT OF NONSPECIFIC ULCERATIVE COLITIS WITH AUREOMYCIN*†

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During the past two years thirty-eight cases of active nonspecific ulcerative colitis were treated with aureomycin. Thirty of these cases have been reported elsewhere[1,2]. Follow-up studies are reviewed on these thirty cases and eight additional cases are presented.

Great caution must be exercised in evaluating the therapeutic effects of a new drug in the treatment of ulcerative colitis. The natural tendency to spontaneous remission which ulcerative colitis manifests, coupled with the established salutary effects of a sympathetic approach and the enthusiastic presentation of a new drug, constitute factors which must be carefully considered in the evaluation of the results achieved. Our series of thirty-eight cases is not large, but the careful follow-up and study of each case offers some assurance that the results which we are presenting are of statistical significance.

Various etiologic concepts have been presented in nonspecific ulcerative colitis. These have included, among others, allergic manifestations, autonomic nerve imbalance, psychic disturbance, vitamin deficiencies, excessive lysozyme production and infection by a variety of pathogenic organisms. Among the latter, hemolytic and nonhemolytic Escherichia coli, hemolytic and nonhemolytic streptococci, enterococci and Staphylococcus aureus are frequently cultured from the stool[3]. Whatever the original formation of the ulcers may be ascribed to, the breakdown of the mucosal barrier[3,4], and the secondary infection which then develops, determine to a great extent the clinical manifestations experienced by the patient and the serious pathological changes produced in the colon.

To combat this nonspecific secondary infection various chemicals, sulfonamides and antibiotics have been employed. It seemed expedient to study the possible therapeutic effects of aureomycin, whose antibiotic activity extends over a wide range of the bacterial and large virus spectrum[5,6]. In studies directed to the evaluation of oral aureomycin on the bacterial flora of the intestinal tract for preoperative medication[7], small doses were found to reduce all enteric organisms except proteus. Larger doses, ranging to 750 mg. four times a day[8], resulted in the elimination of all culturable bacteria (E. Coli, A. aerogenes, S. fecalis and spores) except proteus, pseudomonas and yeasts, from the intestinal tract within three days. One gram of aureomycin daily will maintain a concentration of 500 to 700 micrograms per gram of stool[9].

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We were led to use aureomycin in the treatment of ulcerative colitis by a fortuitous circumstance. Dramatic results were obtained with aureomycin in a case of pyoderma gangrenosum complicating chronic nonspecific ulcerative colitis[10]. The effects on the condition of the colon in this case were sufficiently impressive to warrant further study of the clinical effects of aureomycin in ulcerative colitis.

Patients, Materials and Methods

The patients represented two series of unselected consecutive cases, most of which had been under observation by one of us (J.A.M.) for many years. All had been studied by the usual methods of x-ray, sigmoidoscopy, stool culture and examination for parasites, so that the diagnosis of idiopathic ulcerative colitis had been established.

Aureomycin was given orally in 250 milligram capsules, one every eight hours. If after one or more weeks there was no change in the clinical course, the dose was doubled. If in several weeks there were significant improvements, the dose was reduced to one capsule, once or twice daily. Occasionally nausea was encountered, and was alleviated or prevented with milk or pepto-bismol, which do not interfere with the absorption of aureomycin. No other drugs were used except occasional small doses of belladonna and phenobarbital. A low residue bland diet was prescribed.

Observations were directed toward the clinical response to the drug. These included, particularly, variation in the number of stools after treatment, presence of blood in the stools, gain or loss of weight by the patient, variation in the sigmoidoscopic appearance and, finally, subjective observation on the patient's sense of "well-being".

The results obtained in Series A, thirty cases, treated between November, 1948 and March, 1950 are summarized in Tables I and II. The results of the follow-up in these cases are listed in Table III.

The significant clinical features of the cases in the second series treated between March and October, 1950 are presented in the following reports, and in addition the data on one case are presented graphically in Figure 1.

Case Reports

Case 1:—J. S., a 35-year old physician, gave a history of bloody diarrhea with 8-9 stools daily, of two weeks duration, under the strain of opening a new office and some trouble with his in-laws. Sigmoidoscopy showed diffuse congestion and many small bleeding points, and barium enema showed loss of haustration in descending colon. Aureomycin 250 mg. every eight hours was prescribed, but the patient admitted taking medication irregularly. The diarrhea continued, but tenesmus was relieved. The patient was urged to take his medication regularly. After one week of controlled treatment the stools became soft, formed and were reduced to two daily.

Case 2:—M. F., a 38-year old male, gave a history of ulcerative colitis of 24 years duration. The onset was at the age of 14, after fright while swimming in

TABLE I

ACTIVE CASES OF ULCERATIVE COLITIS
TREATED NOVEMBER, 1948 - MARCH, 1950
SERIES A

No.	Name	Age	Sex	Duration of Disease	Duration of Treatment	Stools						After Treatment		
						No.		Blood		Character				
						Before Aureomycin	After Aureomycin	Before Aureomycin	After Aureomycin	Before Aureomycin	After Aureomycin	Weight Gained (pounds)	Well Being	Sigmoidoscopy Improved
1	H.M.	39	M	18 mo.	12 weeks	25	2	+	0	Watery	Formed	24	++++	+
2	E.K.	23	F	5 yr.	13 weeks	8	2	+	0	Watery	Formed	20	++++	+
3	J.C.	20	M	14 yr.	13 weeks	13	6	+	0	Watery	Formed	28	++++	+
4	L.M.	21	M	6 yr.	7 weeks	6	3	+	±	Soft	Formed	17	++	0
5	H.M.	19	M	12 mo.	11 weeks	7	2	+	0	Soft	Formed	25	++++	+
6	B.C.	42	M	18 yr.	6 weeks	8	4	+	0	Soft	Formed	9	++++	+
7	E.G.	50	M	2 yr	5 weeks	7	2	+	0	Soft	Formed	0	+++	0
8	J.A.	33	F	5 yr.	4 weeks	9	4	+	0	Watery	Formed	0	++	0
9	S.H.	42	M	1 mo.	12 weeks	3	2	+	0	Watery	Formed	4	++	+
10	R.R.	44	F	4 yr.	3 weeks	10	2	+	0	Watery	Semi-formed	−1	+	0
11	L.R.	45	M	5 yr.	11 weeks	6	2	+	0	Semi-soft	Formed	0	+++	+
12	A.G.	32	M	12 yr.	9 weeks	9	5	+	±	Soft	Semi-formed	0	++	Not done
13	C.C.	28	F	1 yr.	5 weeks	8	3	+	0	Soft	Soft	−12	+	0
14	V.H.	38	F	11 mo.	8 weeks	6	2	+	0	Watery	Formed	8	+++	0
15	D.I.	24	F	7 yr.	2 weeks	14	2	++	0	Watery	Formed	3	+	+
16	E.K.	46	M	8 yr.	4 weeks	6	3	++	+	Soft	Formed	0	+	0
17	T.F.	53	F	6 mo.	4 weeks	25	6	++	0	Watery	Formed	15	++	+
18	E.R.	50	F	3 mo.	8 weeks	10	10	+	+	Watery	Watery	0	0	0
19	L.K.	39	F	13 yr.	4 weeks	8	10	+	+	Watery	Watery	0	0	0
20	B.S.	49	F	18 yr.	7 weeks	8	2	+	0	Watery	Formed	−3	0	+
21	H.W.	60	F	7 yr.	2 weeks	10	2	0	0	Watery	Formed	0	+	0
22	W.Y.	50	M	20 yr.	2 weeks	15	3	0	0	Watery	Formed	0	++	0
23	A.A.	39	F	9 yr.	10 weeks	5	2	+	+	Formed	Formed	10	++	0
24	J.C.	63	M	1 yr.	16 weeks	10	4	+	+	Watery	Formed	0	+	0
25	A.L.	33	F	2 yr.	6 weeks	15	2	0	0	Watery	Semi-formed	−4	+	0
26	E.F.	36	F	5 yr.	2 weeks	6–15	2	+	0	Watery	Formed	0	+	+
27	W.S.	39	M	11 yr.	2 weeks	9	6	++	+	Watery	Watery	0	0	0
28	A.N.	42	M	9 yr.	6 weeks	20	4	++	0	Watery	Formed	11	++	0
29	S.Z.	37	F	12 yr.	2 weeks	8	3	0	0	Watery	Formed	0	++	0
30	D.I.	17	M	2 yr.	4 weeks	8	3	+	0	Watery	Formed	13	+	+

TABLE II
SUMMARY OF THIRTY ACTIVE CASES (SERIES A)
TREATED NOVEMBER, 1948 - MARCH, 1950

	Number of Cases	Percentage
Reduction in bowel movements, 50% or greater	25	83
Reduction in bowel movements, less than 50%	3	10
Disappearance of blood	21 (out of 26)	81
Improvement of well-being	26	87
Greater strength		
Less pain and tenesmus		
Cessation of "accidents"		
Nausea	7	23

TABLE III
FOLLOW-UP ON THIRTY CASES (SERIES A)
TREATED NOVEMBER, 1948 - MARCH, 1950

1. Well	14	21 cases out of 30 (70%)
2. Well, but take occasional aureomycin capsule	4	
3. Well, but take aureomycin frequently to control mild recurrences	3	
4. Improved in general but with recurrences, controlled by aureomycin	5	
5. Not well	2	
6. Miscellaneous	2	
Carcinoma of colon (colectomy)		
Brain tumor (death)		

water over his depth. He was in the hospital for eight months at that time for treatment with transfusions and medicated enemas. Since then, he has had numerous bouts of diarrhea lasting months at a time. At the onset of treatment with aureomycin 250 mg. every eight hours in June, 1950, the patient was having ten bowel movements daily, with much blood and mucus. He was taking kaopectate, one ounce every two hours. He had taken chloromycetin, 250 mg. every four hours several months before, without effect. His barium colon enema showed chronic ulcerative colitis of left colon with many polyps. Proctoscopy showed thickened mucosa with purulent discharge, numerous ulcerations and bleeding points. After one week of treatment with aureomycin, the bowel movements were more formed, but still contained much blood. After four weeks of treatment, the diarrhea persisted and the dosage of aureomycin was raised to 500 mg. every eight hours. Bowel movements were unchanged but pain and tenesmus subsided.

Case 3:—C. B., a 25-year old male, was in good health until eight months ago, when bloody diarrhea started during a period of emotional stress on opening a new business. He had served in the Army in Africa during the war, but had no diarrhea during his service. Barium colon enema showed loss of haustration in the descending colon and proctoscopy showed many small hemorrhagic points. At the onset of treatment he had from 15 to 20 watery bowel movements daily with blood. After one week, he had eight soft granular stools daily with no blood. He has continued to have three to five formed stools daily with occasional blood.

Case 4:—E. I., a 31-year old male, developed diarrhea in December, 1948. A diagnosis of ileitis was made and operation performed at Mount Sinai Hospital (ileotransverse colostomy) in October, 1949. Bowel movements have increased since then, so that when first seen he had 20 to 25 bowel movements daily, with blood. He was too weak to get out of bed. Aureomycin, 250 mg. every six hours, was started. He was hospitalized at University Hospital for two weeks, and bowel move-

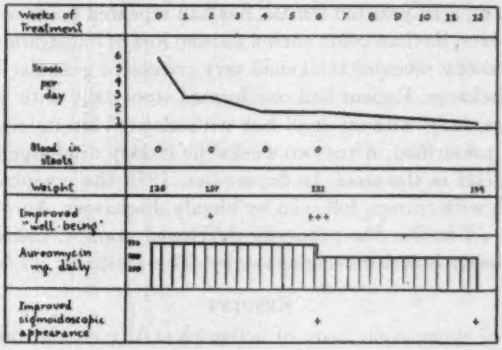

Fig. 1

ments were reduced to six daily with no blood. Since that time he has had 6 to 8 bowel movements each day.

Case 5:—J. F., a 63-year old male, was admitted to Harlem Hospital on March 31, 1950 with a history of diarrhea of two months' duration. Sigmoidoscopy revealed red granular mucosa which bled easily, and many small ulcers. Barium enema showed narrowing and stiffness of the sigmoid colon. Aureomycin, 250 mg. every six hours, was started on April 14. In two weeks there was definite clinical improvement. He had two formed stools daily. Sigmoidoscopy one month after commencement of treatment showed smooth mucous membrane with a few small hemorrhagic points. Dosage was reduced to 250 mg. every twelve hours and then discontinued on June 6. At discharge he felt well and was cheerful. He has been employed in the dietary department of the hospital, and has been well since discharge as a patient. He has two formed stools daily with no blood. Sigmoidoscopy on September 22, 1950 showed no abnormality.

Case 6:—H. P., a 26-year old male, had an onset of diarrhea in December, 1949 with 15 bowel movements daily, little mucus, no blood. He responded fairly

well to sulfasuxidine. In April, 1950 he had another bout of diarrhea which at first responded to sulfathalidine and then recurred. On proctoscopy the mucous membrane was congested with many bleeding points and some ulceration. Aureomycin, 250 mg. every eight hours, was started on June 14, 1950. Within one week he had three semiformed stools daily, no blood. After six weeks of treatment he felt well and had two formed stools daily. Proctoscopy showed slight congestion, no ulceration. Aureomycin was continued in diminished dosage for three weeks longer.

Case 7:—R. G., a 34-year old female, has had bloody diarrhea for five years with frequent exacerbations. Barium enema showed loss of haustrations. Proctoscopy showed diffuse congestion of the mucosa with numerous bleeding points. Aureomycin, 250 mg. every eight hours, was prescribed. In one week the diarrhea stopped and she had one formed stool daily, without blood. A similar attack in September, 1950 with profuse rectal hemorrhage was again controlled with aureomycin.

Case 8:—A. S., a 36-year old female, has had repeated bouts of bloody diarrhea for the past six years. Barium colon enema showed loss of haustration in the descending colon. Proctoscopy revealed thickened very congested granular bleeding mucosa with purulent discharge. Patient had one formed stool daily with blood, and 2 to 3 bloody discharges daily without stool but with clots. Aureomycin, 250 mg. every eight hours, was prescribed. After two weeks the bloody discharge disappeared and there was less blood in the stool. In September, 1950 she complained of blood in constipated stool, with cramps followed by bloody discharges. Aureomycin, 250 mg. was given every six hours. She promptly developed cramps, nausea and vomiting with ten loose bloody bowel movements daily. The antibiotic was discontinued.

Results

This group of thirty-eight cases of active ulcerative colitis treated with aureomycin is divided into two series: Series A, 30 cases, were treated before March, 1950 and were reported previously[1,2]. Series B, 8 cases, were treated between March and October, 1950 and are reported here in detail.

Series A:—A review of Series A (Tables I and II) shows that 83 per cent of the patients experienced a reduction in bowel movements of 50 per cent or greater and a disappearance of blood. Follow-up studies (Table III) showed that 21 cases (70 per cent) were well, 5 were improved, 2 were not well, and 2 had other serious complications (carcinoma of colon and brain tumor).

Series B:—In Series B (see Table V), 6 cases (75 per cent) had a reduction in bowel movements 50 per cent or more. One case had slight reduction. The eighth case apparently had some sensitivity to aureomycin which caused a marked aggravation of the diarrhea and required its prompt withdrawal.

Gross blood was present in the stool of 6 patients. Of these 3 (50 per cent) showed a marked reduction or disappearance of blood in the stool.

A change in the consistency of stools was also observed. All but one of the patients had watery or soft stools before commencing aureomycin therapy. Of these 4 (57 per cent) later had formed stools.

TABLE IV

SUMMARY OF CASES OF ULCERATIVE COLITIS
SERIES B
MARCH TO OCTOBER, 1950

No.	Name	Age	Sex	Duration of Disease	Weeks of Treatment		Stools						After Treatment		
							Number		Blood		Character				
					To Max. Effect	Total Duration	Before Aureomycin	After Aureomycin	Before Aureomycin	After Aureomycin	Before Aureomycin	After Aureomycin	Weight Gained pounds	Well-being	Sigmoidoscopy Improved
1	J.S.	35	M	3 wks.	4	4	7	2	+	+	Watery	Soft	–	+++	–
2	M.F.	38	M	24 yrs.	6	6	18	15	+	+	Watery	Soft	–3	+	0
3	C.B.	25	M	8 mos.	3	8	15	4	+	±	Watery	Formed	–5	++++	–
4	E.I.	31	M	1½ yrs.	2	6	25	6–8	+	0	Watery	Soft	–	++	–
5	J.F.	63	M	2 mos.	2	5	8	2	0	0	Watery	Formed	–	++++	+
6	H.P.	26	M	6 mos.	2	6	6	2	0	0	Soft	Formed	8	+++	+
7	R.G.	34	F	5 yrs.	1	1	3	1	++++	0	Watery	Formed	0	++++	+
8	A.S.	36	F	6 yrs.	1	1	1	10	+++	+++	Formed	Watery	0	0	0

In general a sense of well-being accompanied the reduction in the number of bowel movements and disappearance of blood in stools. Seven cases (87 per cent) indicated a substantial improvement in sense of well-being.

Three of the eight cases (37 per cent) showed improvement in the sigmoidoscopic appearance. This was manifested by reduction in congestion and edema, decrease in bleeding points and less granular appearance of the mucosa.

Combined Series:—Thirty-eight cases.

TABLE V

RESULTS - SERIES B

EIGHT CASES TREATED MARCH - OCTOBER, 1950

	Number of Cases	Percentage
Reduction in bowel movements,50% or greater	6	75
Reduction of blood in stool	3 (out of 6)	50
Improvement of well-being	7	87
Nausea	0	0

A review of the combined series of thirty-eight cases (Table VI) shows that thirty-one (82 per cent) had a reduction in bowel movements of 50 per cent or more, twenty-four out of thirty-two (75 per cent) showed a disappearance of blood in stool, and thirty-three (87 per cent) had a substantial improvement in well-being.

TABLE VI

COMBINED RESULTS SERIES A AND B (THIRTY-EIGHT CASES)

NOVEMBER, 1948 - OCTOBER, 1950

	Number of Cases	Percentage
Bowel movements reduced 50% or more	31	82
Blood in stool reduced	24 (out of 32)	75
Improvement in well-being	33	87
Nausea	7	18
Burning of rectum	1	2.6

PLACEBOS

In an effort to determine the specificity of aureomycin in the treatment of ulcerative colitis, we were led to use placebos. In four patients who had obtained benefit from aureomycin, a capsule identical in appearance to the aureomycin capsule was substituted, unbeknownst to the patient. By this means we hoped to determine whether it was aureomycin or just yellow capsules that helped the patient.

This course was suggested by an earlier case, at a time when aureomycin was difficult to obtain. For about two weeks the patient had no aureomycin, and bowel movements increased during this period.

Four patients were treated with substitution capsules and in three of these the above phenomenon was duplicated. There was an increase in bowel movement and change in the sense of well-being. In short, the patient suffered a relapse. Symptoms were controlled by the replacement of aureomycin for its placebo.

Toxic Effects and Side Reactions

Two cases (L. K. and A. S.), after initial improvement with aureomycin, complained of cramps, and bowel movements were increased. The possibility of a toxic or allergic response is suggested by prompt improvement with the withdrawal of aureomycin.

Seven cases (18 per cent) complained of nausea. At first aluminum hydroxide gel was given with the aureomycin, but this was stopped when it was shown that it reduced the effective absorption level of aureomycin. Milk or pepto-bismol did not interfere with the absorption of aureomycin and did relieve nausea effectively.

One patient complained of burning in the rectum during the course of treatment with aureomycin.

Evaluation

The difficulty in evaluating the response to any mode of therapy in nonspecific ulcerative colitis is well known. Marked response is noted to psychologic factors and there is a natural tendency to spontaneous remission. The high degree of response to aureomycin obtained in these unselected cases is encouraging, and suggests that the possible control of infectious factors may favorably alter the course of the disease.

Summary and Conclusions

1. Thirty-eight cases of active ulcerative colitis were treated with aureomycin in doses averaging 250 mg. every eight hours. Thirty-one (82 per cent) showed reduction in bowel movements of 50 per cent or more.

2. In twenty-four out of thirty-two cases (75 per cent) gross blood in stools disappeared.

3. Thirty-three patients (87 per cent) reported significant improvement in the sense of well-being (including greater strength, less pain and tenesmus, and cessation of accidents).

4. Gain in weight (3 to 28 pounds) was reported in fourteen patients (37 per cent) during treatment. Weight loss occurred in six patients.

5. The sigmoidoscopic appearance was improved in fifteen of thirty-four patients (44 per cent).

6. Six to twenty-four months follow-up of thirty cases previously reported showed twenty-one cases (70 per cent) to be well, five improved, two unimproved, and two with miscellaneous malignant tumors.

7. Four patients whose diarrhea was controlled with aureomycin were given placebos, and the diarrhea promptly recurred in three. Improvement again was manifest by replacement with aureomycin.

8. Nausea was experienced by seven patients. This was controlled by milk or pepto-bismol which do not interfere with absorption of aureomycin.

9. Little if any resistance is built up to aureomycin in the treatment of ulcerative colitis.

10. While the results here reported are most encouraging, continued caution is urged in interpreting the ultimate value of aureomycin in ulcerative colitis therapy.

11. When medical management fails in the presence of gross pathological changes, surgery is indicated.

12. In our experience, aureomycin is the most satisfactory drug now available for the treatment of chronic idiopathic ulcerative colitis.

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THE USE OF AUREOMYCIN IN AMEBIASIS*

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Amebiasis has presented a clinical problem for many years. When so many remedies are offered for one disease we may be certain that none of them are entirely satisfactory.

Until recently amebiasis was considered a disease of the tropical or subtropical regions and even today many clinicians fail to take serious consideration of the large incidence of this condition which is undoubtedly prevalent, to some extent, in every part of the United States.

The introduction of emetine in 1912 was a considerable advance over the previous treatment with ipecac and colonic irrigations with quinine. In 1921 chiniofon was introduced; bioform in about 1931 and diodoquin in 1936. The first of the arsenicals, stovarsol, appeared in 1923. This preparation was highly toxic and a much less toxic arsenical, carbarsone, was introduced shortly thereafter. In 1949 chlorquine, a derivative of the 4 amenoquinoline series was introduced. It has the properties of almost complete absorption from the gastrointestinal tract and extensive localization in the liver. This latter preparation appeared to be an effective agent for amebic infection of the liver . . . certainly as effective as emetine but far less toxic. Even more recently introduced are 2 thiorsenites (dithiocarboxymethyl and dithiocarboxyphenyl). These agents are many times more effective than carbarsone and appear to give greater distribution of the active amebicide to the intestines and the liver. Another arsenical, bismuth glycolylarsenilate, has been used in Europe recently, but I have no authentic record of its use in this country. Needless to say, all of these arsenicals are, to an extent, dangerous and need to be used with caution.

Insofar as I am able to determine, the first radical departure from the use of iodides and arsenicals was made in my home city of Memphis, Tennessee. This work was done at the John Gaston Hospital by Dr. Leon McVay, Jr., a Resident in that Institution. This original work was reported in November, 1949[1].

McVay reports that while using aureomycin in the treatment of various infections a change was noted in the gross character of the stools and subsequent microscopic examination revealed an alteration in the fecal bacterial flora. It was accordingly decided to try aureomycin in the treatment of amebiasis. The results were entirely satisfactory in 36 of these cases which remained free of infection as evidenced by repeated stool examinations over a period of six months.

Being somewhat impressed by the results obtained at the John Gaston Hospital, I began using aureomycin in my private cases in December, 1949. Using a dosage of 250 mg. every four hours for four doses and an additional 250 mg. for

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every six hours thereafter, encouraging results were noted in the first few cases treated; subsequently, however, the amount of aureomycin was increased to 2 grams daily for one week. Such a procedure was followed by no untoward reactions and the dosage was continued at 500 mg. of aureomycin administered orally four times a day for one week, given about one hour after meals and at bedtime. On a few occasions patients complained of nausea, but there were no cases of severe gastric upset. Cases that did complain of nausea were given mild sedation which invariably reduced the disagreeable symptoms to the point of comfort. An occasional patient complained of tenseness or anxiety, but in no case were patients incapable of continuing routine medication. In cases of severe nausea prompt relief was invariably experienced after the intravenous administration of 100 mg. of pyridoxine. This, of course, requires hospitalization but it is well worthwhile to hospitalize a patient for a week in order to obtain which appears to be permanent relief.

Another internist, Dr. John Davis Hughes, of Memphis had an article in The Journal of the American Medical Association on April 8, 1950[2], wherein he reports the treatment of 38 patients with aureomycin with a 71 per cent recovery. These patients received 28 capsules (0.25 gm.) over a period of 4 to 7 days. In the light of recent experience I think that his percentage of cures would have been much higher had he used a larger dosage.

In my own practice I have treated and have been able to follow up 34 cases since December, 1949. In every instance patients given the full dose of 2 grams of aureomycin, in divided doses over a period of one week, reported prompt cessation of symptoms which had originally varied from mild digestive discomfort to frank and frequent diarrhea.

I might add that the administration of B-complex, in large doses, given during and immediately after the administration of aureomycin has a tendency to offset some of the undesirable side effects of this drug.

I have had the opportunity of observing only one case with an amebic abscess of the liver and promptly lost track of this man after his initial visit. I can, however, see no reason why an agent giving such dramatic results with ordinary amebic dysentery should not be effective in cases of hepatic amebiasis. The criteria of a cure in amebiasis is, of course, the absence of parasites or cysts in the stool after repeated examinations. In each instance reported, such a procedure was used but it is, perhaps, a little early to claim a cure in all cases under my observation.

Freedom from symptoms over a period of ten months, does not necessarily mean that a case of amebiasis is thoroughly cured, but I will say that the absence of symptoms of recurrence in a series of 34 cases is far more encouraging than results heretofore obtainable with the previous conventional procedures with emetine, iodides and arsenicals.

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Discussion

Dr. Henry A. Monat (Washington, D. C.):—I was very much interested in the paper on Aureomycin in Amebiasis. In my practice in Washington I have the opportunity of treating cases of amebiasis from all over the world and I, too, have come to the conclusion that aureomycin is the least objectionable drug to take with the maximum percentage of cure.

If I fail with aureomycin on my first course, I try for the second one aralen and milibis.

As a warning, I would like to emphasize two things: 1) there should be five stools in succession and rectal washings on all suspected cases of amebiasis; 2) All suspected cases should have a complement fixation test.

Dr. Horace W. Soper (St. Louis, Mo.):—My experience with amebiasis occurred after the great epidemic in the Chicago hotel where the water supply was infected by a carrier and there were hundreds of cases, fifty of them that I saw in St. Louis. A number of my cases occurred from New Orleans, from infection in the oyster bed, to the number of twenty-five, so I had seventy-five cases to report. I did report them some time ago, but my treatment, briefly, was this: For seven days, one grain of emetin (Burroughs, Wellcome & Company) intravenously, not subcutaneously—intravenously—for seven consecutive days, followed the next week by a dose of stovarsol three times daily before each meal, for one week; no other treatment after that.

All made complete recoveries, and there was never a single recurrence. Most of these cases, of course, were acute ones, that I saw early, in which I could make a diagnosis very easily, when it was missed in the stool specimen, by a swab, collecting the mucus just above the sphincter ani where the mucus collects. A swab will nearly always show the ameba.

IS SURGERY NECESSARY FOR THE SILENT GALLSTONE?*

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The presence of a gallstone is a pathological finding. For the patient with definite symptoms that can be attributed to the presence of gallstones within an ailing gallbladder surgery is the universally accepted treatment of choice. But surgery for the "silent" gallstone is far from being accepted as the treatment of choice. Therein lies the field of controversy.

Gallstones have been said to vary in occurrence from about ten per cent in all age groups, thirty per cent in middle life, and up to seventy per cent of all autopsies over the age of seventy. Infancy is not immune to this pathological finding. Gallstones are found more frequently in women, ranging up to four times its occurrence in men. Predisposing factors are obesity, gout, diabetes, diet, sedentary work, bedrest, blood dyscrasias.

The etiology of gallstones in the present state of our knowledge is based wholly on theoretical assumption. The usual causes credited for gallstone formation are (1) disturbed cholesterol metabolism, (2) endocrine disturbance, (3) stasis, (4) infection, (5) reflux of pancreatic juice. High blood cholesterol has been indicated as a factor in gallstone formation. Again, sudden changes in the cholesterol or chemical make-up of the bile contained within the gallbladder are frequently given as adequate cause for chemical crystallization and gallstone formation. The endocrine changes that occur with pregnancy and the menses, together with the pituitary, adrenals and thyroid have been set down as playing an important role in calculus formation. The regurgitation of pancreatic juice with subsequent slough and erosion of the gallbladder has been given credit by some investigators for the formation of stones. The elimination of fats from the diets of the obese in their attempt to lose weight is a noteworthy example of a cause of gallstone formation. It is felt that infection of the gallbladder may play a definite part in stone formation.

Gallstones may occur as pure cholesterol stones or as a compound or mixture of the bile constituents.

The presence of gallstones may or may not give rise to symptoms. Bockus attributes to Rothman the statement that only one in every ten patients with gallstones has symptoms. Truesdell found gallstones in ten per cent of five hundred women not suspected of having stones. Robertson made a careful study of the clinical histories of 1,027 autopsies at the Mayo Clinic in whom gallstones were found. He concluded from this study that in sixty-one per cent neither the attending physicians nor the patient were aware of the presence of gallstones.

The symptoms of gallstones vary. The classical attack of colic with or without jaundice is known to all. The severe pain of acute cholecystitis or the

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dull ache of chronic gallbladder disease are frequently due to the presence of stones in the gallbladder, although such complaints may exist without the presence of gallstones. Rehfuss assumes that belching, unstable colon, and constipation are a definite part of the gallbladder picture.

It is not unusual to find unsuspected gallstones in the course of a routine check-up of a patient whose complaints are nonexistent or are far afield from the abdominal area. When gallstones are found under such circumstances the question of therapy arises. Shall we advise immediate extirpation of the gallbladder? Upon questioning many of these patients closely, some of the so-called silent gallstones are not so silent. But there is always a considerable percentage of cases in whom no amount of suggestive prodding or skillful questioning can uncover any symptoms relative to the gallstone that has long made its home within the gallbladder of the unsuspecting host. No medication of any type is indicated, and no diet is necessary. How can one be justified in suggesting surgery—and how many of such patients would submit to surgery? True—one can fortify himself with statistics that indicate the mortality rate for cholecystectomy as about two-tenths per cent in uninfected cases in young individuals, to about two per cent in the more advanced cases and in older individuals and complications become more frequent as the years go by. The unsuspected uninfected gallbladder may become infected so that now cholecystitis, empyema, cholangitis, liver and pancreatic pathology, perforation of the gallbladder and peritonitis, fistula, intestinal obstruction, and malignancy make themselves evident with the increasing age of the patient.

With the above thoughts in mind a questionnaire titled "Is Surgery Required for a Silent Gallstone?" was sent to a group of nationally prominent surgeons and internists to get a cross section opinion on this controversial subject. The questionnaire produced some very interesting observations by many men whose opinions are highly respected by the medical profession at large. Of the forty answers received, ten surgeons felt that no surgery was necessary for the silent gallstone, while twenty surgeons were in favor of operation. Four internists were opposed to operation and four favored surgery, two internists hedged on the question. It would therefore appear that two-thirds of those answering the questionnaire were in favor of cholecystectomy for removal of silent gallstones. However, the answers did not always show a clear-cut decisiveness and were restricted to a final decision based upon other factors present in the individual case. From all the replies received the following is a composite list of the important factors necessary in the evaluation of the individual case: (1) Presence of infection. (2) Age of the patient. (3) Prophylaxis against complication of infection. (4) Function of the gallbladder. (5) Availability of competent surgery. (6) General physical condition of the patient. (7) Prophylaxis against malignancy. (8) The size and quantity of stones. (9) Is a silent stone really silent?

Many of the replies were colored by the experience of the physician. Thus, Pack, who confines his work "To the Study and Diagnosis and Treatment of Cancer" indicated that: "almost every cancer of the gallbladder he encountered had gallstones associated with it", and since "the incidence of cancer developing

on the basis of gallstones is greater than the operative mortality for cholecystectomy" he advocates surgery for all gallstones. Lahey believes that most gallstones are not silent and that the proper time for operating on the patients for gallstones is when they are not having symptoms. Carter insists upon cholecystectomy when duodenal drainage shows an infectious organism in the presence of a silent gallstone. Alvarez is inclined to leave a silent gallstone alone if the patient lives in a community where adequate surgery is always available. Hinton is absolutely opposed to surgery for the silent gallstone. Crile best answers the question by stating that if he himself had a silent gallstone he would not permit himself to be operated upon. Charles Mayo prefers to temporize with the silent gallstone recommending caution and periodic examination. Burke at the Jersey City Medical Center has seen a tremendous amount of surgical complications arising out of gallbladder pathology and he is therefore quite emphatically in favor of early prophylactic cholecystectomy.

In spite of the pro and con opinion one thing is certain, the bane of the gastroenterologist's practice is the postcholecystectomy syndrome, the waste basket diagnosis frequently given the patient who has submitted to cholecystectomy and who now comes to plague us with descriptions of varied symptoms for which we can frequently find no explanation, rarely find good medical treatment, and not too rarely we seek an explanation for it by a second or even a third surgical exploration. With such cases of disability following gallbladder surgery it is indeed hazardous to advise a cholecystectomy for a silent gallstone discovered accidentally and giving rise to no symptoms. Indeed I venture to say that most physicians who have had the opportunity of following patients with silent stones or for that matter that are not so silent, are surprised at how small a percentage of these with good medical management and observation actually become surgical emergencies. In a personal follow-up of about one hundred such cases over a period of twenty years I have not had one surgical emergency.

One can also carry a serious situation to a point of absurdity. Granting the medical maxim "prophylaxis is the best cure" it might be wise to take out every gallbladder one can lay hands on, stone or no stone. For if seventy per cent of all gallbladders contain stones at the age of seventy, and since the longevity rate is constantly increasing, then at the age of one hundred, to which it appears a larger and larger percentage of us is going to live, one hundred per cent of all gallbladders should contain stones. Therefore, why not do surgery at a more practicable age, rather than wait for the inevitable formation of gallstones and all the complications they may breed.

My answer would be "No" to the question "Is Surgery Necessary for the Silent Gallstone?". There is a great lack of unanimity of opinion on the part of the medical profession as to the proper treatment of the silent gallstone. Each case should be individualized and the sum total of our experience and knowledge of the problem must be weighed against our findings and the complaints of the patient. One must be certain that the gallstone is silent. And we next must consider the potentialities of the presence of such a stone or stones in the gallbladder. The

future possibilities of infection and the complications that follow such infection must be kept in mind. Malignancy of the gallbladder is practically always associated with stones and therefore malignancy cannot be disregarded. On the other side of the scale are the morbidity and mortality rates. I am not anxious to treat a postcholecystectomy syndrome in a previously symptomless patient nor would I receive with enthusiasm the autopsy report on a previously well individual who incidentally harbored a silent stone. It would appear that an opportunity does exist to practice preventive medicine when cholecystectomy is advised for silent gallstones in a patient under forty whose general condition is excellent. However, one must be prepared to face an ailing and perhaps irate patient who had no previous abdominal complaints. After a few such patients have worn out the carpet in your office a conservative attitude toward the silent gallstone will soon become most popular with you. From a practical viewpoint therefore it seems to me that very few patients would submit to cholecystectomy for silent gallstones and we as physicians can, with a clear conscience, postpone surgery indefinitely if the patient agrees to remain under medical observation and care, and lives where good surgery is easily obtainable if an emergency should arise.

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Crile, George: Personal communication.
Burke, Edgar: Personal communication.
Mayo, Charles W.: Personal communication.

Discussion

Dr. Lester R. Whitaker (Portsmouth, N. H.):—It seems to me that the confusion of ideas with regard to the treatment of the pathological condition of gallstones comes from inadequate understanding of the physiology and pathology of the gallbladder. Briefly, the gallbladder contracts muscularly after eating fat. The gallstone, not infection, is the primary disease. It produces secondary disease by obstruction.

Dr. Riese, while respecting your opinion, I wish to disagree with you with all the emphasis at my command. After twenty-five years of study of the gallstone, silent, howling, or screeching, I have come to the conviction that, like the Moscow communist in our midst, the gallstone is a dangerous enemy, plotting the destruction of his host. Like the silent, smirking Joe, he carries a weapon ready to inflict a

stab in the back which may be mortal. With the gallstone, as with the Moscow communist, the only safe place for him is a basket or a box.

This is the reason: The gallbladder is a contractile sac, tapering to a small, tortuous outlet which may be only 2 mm. in diameter and easily blocked. During the normal contracture of the gallbladder after eating, the stone may wedge wherever the passage becomes too small. I have seen obstructing stones from 2 mm. to 5 cm. in diameter.

While the stone, like the communist, is floating around, he is apparently harmless, but waiting the right time and place for his nefarious deed. The gallstone, silent or screeching, should be removed. There is only one doubtful case, the patient with one foot in the grave; and many times even in such a case, modern surgery, with the ways and means at its command, can drag that foot back and place it on solid ground.

Dr. B. O. C. Pribram (New York, N. Y.):—It is generally not realized that the term "silent lithiasis" does not cover something mysterious and hard to explain. We have fairly good knowledge as to why a gallstone, lying in the gallbladder, is sometimes silent, and sometimes becomes a great nuisance.

Perhaps I can explain to you what I mean: I had a patient with a cholecystostomy. In introducing a probe into the gallbladder, I could touch and scratch the mucous membrane of the fundus as much as I liked. The patient did not feel a thing, but as soon as I came with my probe to the opening of the cystic duct, or tried to force the probe in the opening of the cystic duct, the patient immediately experienced colicky pain radiating to the back and even to the shoulder. This pain subsided immediately on withdrawal of the probe.

Translated into the clinical language of cholelithiasis, this means as long as stones lie in the fundus, they are silent; as soon as they move in the cystical area a colicky pain sets in.

The moving of stones into or passing through the cystic duct is the actual basis of a typical gallstone attack, while the passing of a stone through the papilla may be completely painless. I could satisfy myself of this generally unknown fact repeatedly when after dissolving of an obstructing common duct stone by means of the ether method I could pass my rubber tube to and fro through the papilla into the duodenum without the patient feeling anything at all.

We may say that gallstones are like dogs: the smaller they are the more noise they make. This is definitely true of small stones that may easily enter the cystic duct and become a terrible nuisance, while large stones are not so easily shifted around, and may lie for years silently in the fundus of the gallbladder. However this does not mean that large stones are less dangerous, but like big dogs they often do not bark at an approaching danger. They have their own way of causing most dangerous complications, which, however, also may remain silent until the patient is admitted to a hospital as an emergency with the signs of an acute abdomen, the etiology of which often is revealed only at operation. Such complications are: hemorrhagic infarction and gangrene of the gallbladder, rupture into the free abdominal cavity, or into a neighboring viscus leading to a gallstone ileus. I wish to

mention only two instances: a man of 60 years of age with a rupture of a large stone into the prepyloric part of the stomach, admitted to the hospital for intractable vomiting and a man of 75 operated on as an emergency for a gangrenous gallbladder, which contained a large stone the size of a chestnut. This man during all his life never had had any symptoms not even of the slightest indigestion. He was always a strong eater and drinker. Now, as to the indications for surgery in case a lithiasis has been discovered by chance during a routine examination. Obviously it boils down to the question whether or not to operate for prevention of a potential danger.

It is my practice to explain to the patient exactly the underlying pathology and the potential dangers and to warn him to be alert to the slightest signs which may indicate a change in the silent position of the stones. This has proven to be good practice because knowing that their stones are on the move when after years of a silent lithiasis they suddenly feel some pain or discomfort in their gallbladder, the patients do appear and ask for surgery, without any persuasion. Others used to choose the time for surgery according to their professional convenience but most of the patients had sense enough to understand that there was no other treatment than surgery and that only the choice of the time for the operation was left to their discretion as long as the lithiasis was silent.

However in the case of a large stone, considering the frequency of absence of any premonitory signs until an acute abdomen was in full development I think it is wise to insist on an early operation as soon as the diagnosis is established.

Dr. Horace W. Soper (St. Louis, Mo.):—Silent gallstones—silent gallstones—we all remember Lyon's biliary drainage to correct it, and we all found out afterwards that magnesium sulfate was not absorbed in the stomach but passed on down and did the same work that the long-continued drainage did; therefore we gave our epsom salts or magnesium sulfate by mouth.

Now, for the active gallstone, of course, surgery is always indicated. For the silent one, if that patient wishes to adhere to a low cholesterol diet and take a small dose of epsom salts every morning, fine—he will go along all right.

I have had many patients who have had cardiac lesions, who were not fit subjects for operation, in whom that treatment was very effective in active gallstones.

SURGERY IN MASSIVE HEMORRHAGE OF THE UPPER GASTROINTESTINAL TRACT*†

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Surgery has a small but very definite and important place in the treatment of massive hemorrhage from the upper gastrointestinal tract. It is generally conceded that the majority (90 to 95 per cent) of cases of bleeding from this area will recover under medical treatment, 5 to 10 per cent according to Heuer will die if surgery is not instituted. Much confusion exists in determining the criteria for surgery. This, I think, is due in part to a lack of agreement of what constitutes massive hemorrhage. Perhaps it would be advisable where surgery has to be considered, to change the term to exsanguinating hemorrhage. Surgery is only indicated in those cases where the loss of blood is so great as to cause syncope, shock and we should realize that death will occur if the bleeding is not checked.

What constitutes massive hemorrhage? Opinion, even now, varies from a drop in red cell count to 3,500,000 to 2,000,000 or 2,500,000 (Bohrer, Stewart) with a corresponding drop in hemoglobin.

Because of this difference of opinion, indications for surgery and mortality figures have varied. Bohrer in 1941 reported a mortality of 45 per cent. In the past, some have placed mild gross hemorrhage in the same category as exsanguinating hemorrhage. Frequently there was no attempt to separate them into groups, such as age and duration of hemorrhage, the type of operation or the stage at which operation was performed, particularly after prolonged bleeding under conservative management.

Hospitals with an ambulance service have a higher percentage of exsanguinating hemorrhages. Some may die at home or in the emergency room and may not be included in mortality statistics. A low hemoglobin and red count may mean significant bleeding but does not necessarily mean that it is of the acute profuse type that endangers life.

The rate of bleeding and the patient's ability to adjust himself to the acute anoxemia is the most important factor in determining whether medical treatment should continue or that surgery is indicated. This has been emphasized by Dunphy et al, hence, there should be the closest cooperation between the gastroenterologist and the surgeon in all cases of hemorrhage from the gastrointestinal tract.

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The Effects of Hemorrhage

Massive hemorrhage results in a diminution of the blood volume, anoxemia and hypotension which is in direct ratio to the amount and rate of blood loss and the adaptability of the individual to this loss. The body makes every effort to preserve the vital centers, even at the expense of other important organs (Wigger). It does this by vasoconstriction to reduce the size of the vascular bed to compensate for loss of volume, and it also mobilizes cells from certain depots, notably the spleen. This in turn is followed by a gradual shift of plasma fluid from the tissues into the circulation. If the blood pressure falls below certain critical levels, the vasoconstrictor center weakens and loses tone because of impaired blood supply and the hypotension increases.

Prolonged hypotension, with qualitative and quantitative alterations in the circulating blood, causes severe anoxemia and serious changes in the metabolic and enzymatic processes, with serious changes in all the vital organs. Cerebral involvement is shown by stupor, dulling of the sensorium, coma, convulsions may occur and the medullary centers may be irrevocably damaged, due to inadequate nutrition.

A unilateral or a bilateral Babinski may be present; cardiac failure or peripheral vascular collapse may follow. Heart damage may be indicated by embryocardia or gallop rhythm, which may be followed by pulmonary edema and death. Pulmonary edema, however, may be due to hemorrhage, even without cardiac damage (Eaton). Angina due to coronary insufficiency may occur. Localized areas of necrosis or myocardial infarction may be present even in young people and without thrombosis. Prolonged low pressure results in the diminishing of glomerular filtration, oliguria, increased nonprotein nitrogen, and blood urea. Gastrointestinal bleeding causes a sharp rise in the blood nonprotein nitrogen in 8 to 10 hours. This is due to absorption of digested blood proteins and prolonged fall in blood pressure, either alone or together. Anoxia increases in direct proportion of the loss of blood and fall in cardiac output and affects all organs. It is worse in the kidney because vasoconstriction is more severe in the renal circulation than in any other vital organ (Fishberg). Hence, in these cases, if they withstand the hemorrhage, they may develop a lower nephronnephrosis.

Moon objects to this term because he feels both upper and lower segments are involved and it should be called acute tubular nephrosis or hemoglobinuric nephrosis.

Sustained increased azotemia in the absence of severe dehydration or preexisting kidney disease occurs with bleeding. The nonprotein nitrogen and urea remains elevated over 24 to 36 hours, then returns to normal, unless the hemorrhage recurs or persists. A urea nitrogen over 100 mg. is usually fatal and associated with symptoms of uremia. The acid base balance is disturbed. The sodium content of the blood is low, but potassium and carbondioxide combining power are increased. There is an increase in the sugar up to 164 mg. or more per 100 c.c. The blood volume shrinks and anemia is present. The plasma protein and plasma volume are decreased but not as markedly as the total blood volume (Stewart).

The liver is affected by anoxia and there is a definite decrease in glycogen, as proven by hepatic biopsy. Frank et al have shown experimentally in dogs, if the liver is vivi-perfused during massive hemorrhage, sufficient protection is given to allow the dogs to survive, however, this is not true if vivi-perfusion is done through the systemic vein. They conclude preservation of the liver function is crucial in advanced hemorrhagic shock.

The function of the adrenals is definitely impeded and the alarm reaction set in motion. The danger is greater over 50 years of age, because (1) local sclerosis of the vessels interferes with retraction and contraction of the vessel. This interference is also caused by the vessel being imbedded in the scar tissue, particularly if perforation occurs in the side walls of the vessel. (2) The inability of the patient over 50 to rapidly adjust himself to the anoxia which is of both the stagnant and anemic type. However, the latter can be controlled by earlier and larger transfusions. Mortality under 30 years of age is 6 per cent and over 50 years is 30 per cent or more according to Finsterer.

Duodenal ulcer causes about 60 per cent, gastric ulcer 12 per cent, esophageal lesion 10 per cent to 20 per cent, malignancy about 4 per cent of all hemorrhages. A certain percentage, as high as 20 in some series, (Crohn) are of unknown origin. Women tolerate hemorrhage better than men. The first hemorrhage carries the highest risk.

Four out of five massive hemorrhages occur in the male. Eighty-two per cent occurred in males and 18 per cent in females, in Costello's series. In Welch's series, 18 per cent were women but they accounted for 21 per cent of the deaths.

The time element is important because danger of death increases with the duration of the hemorrhage, so that after 72 hours have elapsed from the onset, some surgeons refuse to operate because the mortality is so high. Heuer reports a mortality of 70 per cent after 72 hours. However, we feel that these statements are all true to a certain extent, but each case must be individualized. If sufficient blood is given early, and in large quantities, patients over 50 years of age and even after 72 hours, can be operated upon successfully. If early and sufficient transfusions are not done in exsanguinating hemorrhage (Wiggers) a terminal hemorrhagic shock state with persistent lowering of the blood pressure to a low level, tachycardia, hemoconcentration, considerable tissue damage and finally death occurs.

We had one case bleeding for six days, over 50 years of age, who received 16,000 c.c. of blood and was operated upon successfully and a total gastrectomy practically done. The control of anoxia is always the prime requisite.

Diagnosis

One should be reasonably sure that there are no esophageal varices, no interference with the blood clotting mechanism or blood dyscrasias. Ninety per cent of upper gastrointestinal bleeding comes from gastroduodenal lesions, varices or blood dyscrasias. If the history is suggestive of ulcer it is very helpful, however, in the presence of bleeding with a negative history and negative findings, one

may have to give a small amount of barium mixture and have the patient fluoroscoped. Positioning is done by turning the patient from side to side, but no manipulation is used.

Gastroscopy or esophagoscopy may be done to determine the site of the lesion, if shock is controlled. Needless to say, the gastroscopist must be very skillful and fast.

Routine laboratory work includes complete blood count, hematocrit, prothrombin time, blood typing, Rh determination, total blood and plasma volume, blood nonprotein nitrogen and urea nitrogen, carbondioxide combining power and blood chlorides.

In the absence of ulcer history or findings, esophageal varices may be suggested by the presence of spider angiomata on the face, neck and upper part of the body, the reddish-blue discoloration of the thenar and hypothenar eminences, the so-called liver palms, slightly enlarged spleen (this may not be present because the spleen has a tendency to shrink during massive hemorrhage but enlarges later if the bleeding is controlled), sparsity of the axillary and pelvic hair, clubbing of the fingers and a foul breath and gynecomastia in the male.

The prothrombin time is usually below normal in all massive hemorrhage but in liver disease it is apt to be 50 per cent of normal or less. The various flocculation tests are apt to be positive. The easiest test is the bromsulfalein dye retention, as anemia does not affect it but cardiac failure may. There may be a moderate or no increase in dye retention during shock or within an hour or two after recovery from shock, but it is certainly normal after 24 hours. In this test, 5 mg. of the dye per kilogram of body weight is given intravenously and retention estimated after 30 minutes.

A normal excretion (White, Zemchek and Chalmers) during shock usually excludes varices, but a 10 per cent or over, indicates liver pathology. However, one may have a cirrhosis of the liver and duodenal ulcer concomitantly, as we have had. Following recovery from massive hemorrhage, x-ray showed a typical duodenal ulcer, esophagoscopy showed definite varices and liver biopsy showed cirrhosis.

If blood dyscrasias are suspected and the history of ulcer is negative and evidence of liver disease is absent, then platelet count, bleeding and coagulation time, clot retraction time, capillary fragility tests and bone marrow studies should be done.

In the past, we have used the red blood count and hemoglobin as the indicator for operation. This was not dependable, because delay in hemodilution, vasoconstriction and some replacement of cells from the spleen, etc. may give a normal or slightly lessened count and hemoglobin for some hours, consequently, not reflecting the true condition. Then we adopted the rule that any patient that had had a second massive hemorrhage in 24 hours, should be operated upon, this was also unsatisfactory. We feel that the rate of bleeding as emphasized by Dunphy, and the patient's reaction to bleeding and large transfusions, will give us the principal indications for operation. The clinical indications are more

important than the laboratory, although the latter are very helpful, particularly the hematocrit and the circulating volume. We feel that surgery is definitely indicated in:

1. Cases that have been transfused, the initial amount being 1,000 to 2,000 c.c. and if shock or syncope occurs immediately, as soon as the transfusion is finished. The pulse is usually 130 or more and the blood pressure difficult to maintain at 90. The hematocrit is usually under 30. Here blood volume studies show under 60 per cent of normal or less.

2. Cases who have had a serious loss of blood have been in shock at the onset, but, after initial transfusion of 1,000 to 2,000 c.c., apparently stabilize but fail to maintain a circulatory equilibrium with 500 c.c. every 8 hours, but go into shock in spite of this because of continued bleeding.

3. Cases who have early and large transfusions, in spite of having shock at the onset, apparently have recuperated but have a recurrent hemorrhage in 48 hours, as evidenced by reappearance of syncope, shock, etc.

4. Cases that have early and adequate blood replacement even though shock does not recur, who progressively deteriorate, with elevation of the pulse and slow but progressive drop in blood pressure and blood volume.

5. Cases of acute perforation associated with hemorrhage, should be operated upon as soon as adequate blood replacement has been given.

The following cases should be watched very closely for the possibility of surgical interference:

1. Cases that have hematemesis, the outlook is always worse than with melena.
2. Cases with known gastric ulcers.
3. Those who hemorrhage while under strict medicinal treatment.
4. Those cases of hemorrhage associated with pain, because the latter may be either due to impending perforation or penetration, and the latter may involve one of the larger vessels, such as the gastroduodenal.
5. In cases of pyloric obstruction hemorrhages are apt to be much worse.
6. Those over 50 years of age.
7. Those who do not have exsanguinating hemorrhage but who have a prior history of ulcer with previous hemorrhage.

Stewart suggests we should try to recognize early those who will not respond to conservative treatment, and then operate in all cases who have had a massive hemorrhage as shown by the presence or history of shock, within one week prior to admission to hospital, complete blood count of 2,500,000 or less, hemoglobin 35 per cent and the circulating volume 60 per cent or less.

Blood Volume

Total blood and plasma volumes are fairly accurate guides to the amount of blood lost and if repeated, will tell whether bleeding has stopped or is continuing. The volume of blood lost is definitely determined and if further bleeding takes place, the blood volume must lessen in proportion, because we are measuring total volume and total hemoglobin.

The Evans blue dye test is used to determine the total plasma volume (the estimation made by electrophotometer and concentration of dye in plasma read). The blood is taken from the vein in the opposite arm, ten minutes after the dye was injected in the other arm. The total volume is calculated from total plasma volume and hematocrit. If the test is repeated at intervals, it may predict whether shock is or is not impending. It also acts as a guide as to the amount of blood needed for replacement.

The dye method has been criticized as being inaccurate and it is inaccurate if one tries to estimate blood volume to the last decimal point. However, the changes in total plasma volume and total hemoglobin are so great, that the inaccuracies are negligible (Gregersen) because of its great clinical value.

Lipemia may interfere with this test, particularly in ulcer patients who have been on a milk and cream diet. However, in exsanguinating hemorrhage, usually nothing by mouth is given for several hours, or if so, milk is omitted for the same period of time and lipemia will have disappeared. The Evans blue dye test should be done after the bromsulfalein, otherwise it will interfere with the latter test.

Rush has emphasized the above because of its usefulness. Our own series of blood volume studies will be published at a later date.

Cases of Surgical Treatment of Massive Hemorrhage

We have had nineteen cases in all, as follows: Leiomyoma of stomach—Juxta-esophageal (1); Gastric polyps (1); Hypertrophic gastritis (1); Diaphragmatic hernia (1); Leiomyosarcoma of 3rd portion of duodenum (1); Carcinoma of duodenum, 3rd portion (1); Diverticulum of the stomach (1); Acute perforation of duodenal ulcer with massive hemorrhage (1); Acute perforation of gastric ulcer with massive hemorrhage (1); Gastrojejunal ulcer following gastroenterostomy (2); Duodenal ulcer (7), one died; Gastric ulcer (1). All were operated on while actively bleeding.

Mortality

It is obvious that these cases, according to our criteria, were among the 10 per cent destined to die under medical treatment. They represent a small percentage of cases of massive hemorrhage of the upper gastrointestinal tract. We readily can see that conservative treatment is indicated in 90 per cent to 95 per cent of the cases. Two cases out of nineteen died.

1:—W. F., a 24-year old white male, died immediately postoperatively from the effects of continuous hemorrhage for ten hours prior to operation and prior to our seeing him; he had three consultations. This was a desperate attempt to control exsanguinating hemorrhage, a case in a patient who could not be stabilized by continuous transfusions via two extremities.

2:—J. E., a 64-year old white male, with a massive hemorrhage and acute perforation of a duodenal ulcer, who survived operation but died of peritonitis on the sixth postoperative day. He did not die of the effects of blood loss.

Treatment

Transfusion of whole blood is the keystone of the treatment of massive hemorrhage. If whole blood is not immediately available, then plasma or even normal

saline or glucose (5 per cent) in saline are given intravenously until whole blood is obtained.

Sometimes it is difficult to find a peripheral vein, if so, then any of the above solutions may be given by sternal puncture, or, better still, by way of the femoral vein or arterial transfusion done, particularly if the patients are in poor condition.

Citrated blood may be used but if large amounts are to be given and the quantity used is really huge and varies from 3,500 to 16,000 c.c. (the average is 4,000 to 5,000 c.c.), then fresh whole blood should be used, because large amounts of sodium may be given which may lead to fluid retention and pulmonary edema follows.

S. M., a 50-year old white male saloon keeper, was admitted to the hospital in shock plus hematemesis. He was given massive transfusion, it being started as soon as the typing and cross-matching was done. He had a long history of alcoholism and a short history of digestive disturbance, also aortic regurgitation which had been diagnosed some time previously. X-rays of the gastrointestinal tract, which had been taken some months previous, showed what might be construed as suspicion of duodenal ulcer, but the films were poor and a definite diagnosis could not be made.

Blood volume studies revealed that he needed at least 5,000 c.c. of whole blood to restore the blood volume to normal. He was watched very carefully but it was difficult to keep him stabilized, even with almost continuous transfusion. Because of the long history of excessive alcoholism, paucity of digestive symptoms and the indefinite x-ray findings, we were loathe to operate. At the end of about 15 hours he was stabilized and we had definitely decided to continue conservative treatment. Transfusions were given almost continuously to restore his blood volume to normal. Twenty-four hours after admission the patient developed pulmonary edema which he survived.

Promptly reviewing the treatment to find the cause of the pulmonary edema, we found that he had been given, without our sanction, normal saline intravenously between transfusions, and that normal saline was being used to irrigate the tubing. After adding up the amount of sodium in the blood, the sodium in the sodium citrate and that contained in the saline solution, we estimated he had been given 37 gm. of sodium, in less than 24 hours.

Normal saline is contraindicated when there is severe anemia. Therefore, we feel that the excessive amount of sodium in less than 24 hours, plus a patient with a cardiac lesion, was entitled to pulmonary edema, because these factors and fresh whole blood would have been better.

Again, the large amount of citrate used may interfere with the blood calcium and reduce the coagulation properties. Fresh blood contains a normal prothrombin concentration, normal intracellular potassium, white blood cells and platelets which are necessary and useful.

If shock is present we usually give 2,000 c.c. the first five hundred rapidly, then the rest slowly, watching the pulse and blood pressure every half hour. Blood volume studies and careful estimate of the patient is done. If shock has been

present and the patient has recovered from it, we start transfusions immediately. If blood pressure is below 100, pulse over 100, we try the tilt test of Green and Metheny. This is based on the response of the cardiovascular system to tilting the body to an angle of 75 degrees or more, for three minutes; if the pulse increases 30 or more beats above the rate while supine, 1,000 c.c. of blood is needed. If syncope occurs, then 1,500 c.c. are necessary. A blood pressure of 80 Hg systolic usually represents a blood volume of 60 per cent or less. In shock due to exsanguinating hemorrhage, the blood pressure is usually below 70, pulse 120-130, R.B.C. less than 2,500,000 and hemoglobin less than 6 grams.

Sodium luminal is given to quiet the mental apprehension. Usually nothing is given by mouth in these cases, because they are nauseated and vomit if you do.

The patient is carefully observed and the criteria previously discussed invoked. If operation is decided upon, usually we wait until the blood pressure is stabilized around 90. To stabilize the blood pressure, blood may be given continuously, intravenously in two extremities, and this continued throughout the operation. Intratracheal anesthesia of gas oxygen and ether, or cyclopropane is usually given.

If ulcer is present, subtotal gastrectomy is done. This yields the best results, stopping the bleeding directly and in the majority of the cases removes the cause of the ulcer.

The mortality is fairly low, Stewart reports one death in the last 33 cases in acute exsanguinating cases. We feel that this is the best procedure, having even done total gastrectomy for bleeding gastric leiomyoma at the juxtaesophageal junction. In those where it is technically difficult to mobilize the duodenum, the exclusion operation of Devine has been used or gastroenterostomy has been done and a tampon placed on the duodenum for pressure to control bleeding (Finsterer).

We feel that the suggestion of Welch is very valuable and better than the two preceding maneuvres. We have used it with subtotal gastrectomy, where it was technically impossible to suture the stump safely. This procedure consists in doing a subtotal gastrectomy and inserting a mushroom catheter in the duodenal stump, purse-stringing the wall of the duodenum around it and bringing it out through the abdominal wall. A jejunostomy is also done with the catheter emerging through the abdominal wall, both catheters being connected by a glass tube. In this way the duodenal contents are returned into the jejunum and the usual ill effects of duodenal fistula eliminated. The tubes are removed in 14 days and the fistulae close rapidly.

With massive hemorrhage from gastrojejunal ulcer, subtotal resection of the stomach and resection of the jejunum or repair of the jejunum after the ulcer is excised, is the best procedure. We have done it in two cases.

For benign or malignant tumors of the stomach, subtotal, even total gastrectomy may be done.

For esophageal hiatus or traumatic diaphragmatic hernia causing ulceration and hemorrhage, correction of the hernia will probably suffice, resection may have to be done.

In case C. D., the patient developed a traumatic diaphragmatic hernia as the result of being crushed. Five days later he had a massive hemorrhage from the upper gastrointestinal tract. Operation revealed superficial ulceration and severe congestion of the stomach due to constriction of the stomach by the diaphragm. Repair of the hernia corrected the condition.

In those cases where an ulcer is found (Stewart reports 15 per cent) and varices and dyscrasias are ruled out and if the stomach and upper intestines are filled with blood, one may open the stomach, wash it out with saline and find shallow ulcers, or, one may not find them except on perfusion of vessels after the stomach is removed. Subtotal gastrectomy is indicated here. We did one case for hypertrophic gastritis.

For benign and malignant tumors of the duodenum, resection is indicated in massive bleeding if the common duct or ampulla are not involved. We have resected the third portion of the duodenum with end-to-end anastomosis in two cases, leiomyosarcoma of the third portion of the duodenum and one adenocarcinoma.

In perforation with massive hemorrhage, ligation of the vessels (pancreaticoduodeno in duodenal ulcer; the left gastric in gastric ulcer) with mattress suturing of the perforation was done.

Summary

1. An effort has been made to clarify the indications for surgery in massive upper gastrointestinal hemorrhage. Clinical signs are most important.

2. Diagnosis is important, particularly to rule out esophageal varices, blood dyscrasias and disturbances of prothrombin mechanism.

3. Blood volume estimation offers an excellent method to determine the amount of blood lost, and if bleeding has stopped, is continuing or is recurrent.

4. Early transfusion of whole blood, preferably fresh, in huge amounts is absolutely necessary.

5. Early operation is essential in exsanguinating hemorrhage. In ulcer subtotal gastrectomy is the operation of choice.

6. Mortality in this group is definitely getting lower. We must remember that in this 10 per cent group the mortality was 100 per cent.

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Discussion

Dr. Frederic W. Bancroft (New York, N. Y.):—I have had the privilege of reading in advance this excellent paper by Drs. Halligan, Perkel, Catlaw and Troast. The authors have covered the field so well that it is difficult for the discussers to criticize their work or to add much of value. I shall therefore emphasize and possibly elaborate on some of the subjects they have mentioned.

I like the attempt to define exsanguinating hemorrhage. Despite any definition, surgeons' opinions will vary as to the amount of blood lost during such a hemorrhage. One might readily draw a parallel to the description of appendicitis with peritonitis as observed through a small incision. One man will describe it as peritonitis if he sees free fluid slightly turbid. Another will call it peritonitis if there is milky, cloudy exudate, and a third will say it is peritonitis only when the intestines are injected and covered with fibrin. How far peritonitis extends from the immediate neighborhood of the appendix and is observed through a reasonable right quadrant incision, it is impossible for anybody to state.

While the blood studies so adequately described give us the best indication for blood replacement, they are not accurate in general. They are the best tests we have, but they do not take into consideration the age of the individual nor the condition of the individual's arteries. A younger person can lose much more blood than one in the older age group and still withstand surgery.

Ravdin has very definitely emphasized the effect on the liver of pronounced anoxemia and the dangers that may ensue if an irreversible condition exists that cannot be benefited by any therapy.

I like the authors' excellent diagnostic description and their suggestion of the bromsulfalein dye retention test to exclude esophageal hemorrhage.

At the Presbyterian Hospital, a recent study by Harold Harvey has shown the great improvement that has occurred in the treatment of gastric hemorrhage, both

medically and surgically, during the past decade. Harvey has analyzed the results of medical and surgical treatment of exsanguinating duodenal ulcer, as follows:

TABLE I

CASES OF SEVERE BLEEDING FROM DUODENAL ULCER
1930-1937

	Number of cases	Number of deaths	Death rate
Medical therapy alone	213	12	5.6%
Medical therapy, plus surgery, elective	20	7	33.0
Medical therapy, plus surgery, emergent	6	4	66.7
All cases of severe bleeding	239	23	9.6%

TABLE II

CASES OF SEVERE BLEEDING FROM DUODENAL ULCER
1948

	Number of cases	Number of deaths	Death rate
Medical therapy alone	45	0	0
Medical therapy, plus gastric resection, elective	16	0	0
Medical therapy, plus gastric resection, emergent	15	1	6.7%
All cases of severe bleeding	76	1	1.3%

TABLE III

CASES UNDERGOING GASTRIC RESECTION AS EMERGENCIES FOR ACUTE HEMORRHAGE*
1941-1947

Case No.	Major Complication after Operation	Result
1	Secondary hemorrhage from ulcer	Died
2	Secondary hemorrhage from ulcer	Died
3	Secondary hemorrhage from ulcer; peritonitis from duodenal stump leak	Died
4	Peritonitis from duodenal stump leak	Died
5	Peritonitis from duodenal stump leak; thrombophlebitis; possible mesenteric thrombosis	Died
6	Cardiac or respiratory failure	Died
7	Gas gangrene of abdominal wall	Died
8	Duodenal stump leak	Survived
9	Duodenal stump leak	Survived
10 to 13	None	Survived

*Ten patients were male; three female.
One was 32 years old; nine between 51 and 60; two between 61 and 70; one was 72.

TABLE IV

CASES UNDERGOING GASTRIC RESECTION AS EMERGENCIES FOR ACUTE HEMORRHAGE*
1948

Case No.	Major Complication after Operation	Result
1	Duodenal stump leak; atelectasis; cardiac insufficiency, temporary; cerebral vascular accident	Died
2	Duodenal stump leak; secondary hemorrhage, controlled by second operation	Survived
3	Probable multiple emboli; severe paralytic ileus	Survived
4	Wound disruption with evisceration; jejunal fistula; operation to relieve these. Mild postoperative bleeding	Survived
5	Secondary hemorrhage, probably from ulcer; massive thrombophlebitis with pulmonary infarct	Survived
6	Biliary fistula (possibly from gallbladder which was opened at operation)	Survived
7 to 15	None	Survived

*Twelve patients were male; three female.
One was 29 years old; one 39; three between 41 and 50; four between 51 and 60; four between 61 and 70; two were 72.

The improvement in the end results is due largely to the extensive use of blood as the therapeutic measure and the generous diets suggested by Andresen or Meulengracht.

In the series from 1930 to 1937, of the thirteen who survived the elective surgical procedure, eight died of complications, two had severe complications but survived, and only three of the thirteen had uneventful convalescences. In the series reported for 1948, one patient died postoperatively, five had very severe postoperative complications, and nine had none. Of the five who suffered severe complications, it is obvious that in a poorly organized hospital the mortality would have been higher.

In cases where the hemorrhage is not absolutely exsanguinating, the buffer solution formula of Grover Penberthy, of Detroit, might help stop the bleeding. This therapy seemed to be the main factor in the recovery of two of my patients, both with fairly severe gastric hemorrhages. In brief, Penberthy recommends a buffer solution of di-sodium phosphate and di-hydrogen potassium phosphate and introduces thrombin. The formula is as follows:

20.4 grams of di-sodium phosphate in 1,000 c.c. of water.
1.95 grams of di-hydrogen potassium phosphate in 100 c.c. of water.
Mix the two together.

Method of administration:—

1. Aspirate the gastric contents on admission by a Levine tube.
2. Instill 50 c.c. of buffer solution and clamp tube for three minutes.
3. Open tube and instill 50 c.c. of buffer solution containing 10,000 units of topical thrombin (Parke, Davis & Co.).
4. Clamp tube for 20 minutes.
5. Aspirate gastric contents. If fresh blood is still present, repeat thrombin. If bleeding is arrested, give 50 c.c. of buffer solution by tube every half hour for 72 hours.

Dr. Penberthy adds that if thrombin is not effective in markedly decreasing the hemorrhage, surgical intervention should be considered without too great delay.

One other factor that has recently been brought out which may help us to save an occasional patient is knowledge of the potassium sodium shift. As you know, sodium is the main metal in extra cellular fluid, while potassium is the main metal within the cell. With repeated intravenous transfusions, starvation, and repeated operative trauma, a potassium shift occurs and unless we are aware of this, we may lose our patient. Use of potassium either by mouth or intravenously in these cases may make the difference between recovery and mortality.

In cases where the bleeding comes from dilated esophageal varices, the use of a Paton tube may help stop the bleeding temporarily until further measures can be utilized. As you know, the Paton tube is a balloon-like tube which has a gastric tube passing through the center and a second cuff. The tube is inserted into the stomach and withdrawn until the cardia grasps the cuff. When the balloon is dilated, compressing the esophageal varices, feeding can be carried out through the tube.

In a recent article which has not had the proof of time, George Crile, Jr. has advocated a transthoracic approach to esophageal varices. He opens the esophagus just above the stomach and does a ligation of the varicose bleeding vessels. He says the looseness of the esophagus renders longitudinal incision and closure easy and he has reported several cases that have gone six months or more. This may be a method in esophageal varices that we have not yet approached.

I should like to suggest one clinical point in intravenous medication. We very frequently use up all available veins but the long saphenous vein may be left because of its inaccessibility. If one makes an incision over the long saphenous in order to put in a cannula in rather a stout person, the cannula comes at right angles to the vein and it is rather difficult to maintain it in position. Whereas if one will expose the vein, make a stab wound two or three inches below the exposure, then pass the cannula up underneath the superficial fat and insert it into the vein at the site of the original exposure, it then lies almost parallel to the vein. The original incision is then closed and one can keep up intravenous medication for a considerable period of time.

I agree thoroughly with the authors that in severe bleeding, fresh blood is better than bank blood, as there is more active prothrombin in fresh blood and therefore greater potentialities of increasing the clotting elements of blood.

The authors have mentioned the pyloric exclusion operation as described by Devine. Later I proposed a modification of the Devine exclusion operation. I should like to state that I think that it is not an operation of choice for hemorrhage.

In hemorrhage we have only one main objective; get the vessels that are causing the bleeding. In duodenal ulcer, unfortunately, this means subtotal gastrectomy. It is a difficult operation to do, especially in a person suffering from hemorrhage, but I can see no other way to control the bleeding, and it is very difficult in duodenal ulcer to expose the arteries and ligate them.

In the lesser curvature of the stomach, one can expose the vessels and ligate them, followed by plication of the stomach over the ulcer. This is not practical in cases of duodenal ulcer.

Finally, I should like to compliment the authors on this excellent paper.

Dr. Hyman I. Goldstein (Camden, N. J.):—Massive hemorrhage may occur from lesions other than ulcer, cancer and polyps. Even some of our ulcer patients may suffer from massive hemorrhage due to other coexisting conditions. Certain blood dyscrasias and dysplasias may give rise to such bleeding. I have reference to patients who have suffered from telangiectatic bleeding—telangiectases in the gastrointestinal tract. Such instances have been observed by me; Ersner, FitzHugh of Philadelphia; B. B. Crohn of New York; Gordon Hein of San Francisco; Leo Kessel and Asher Winkelstein of New York; S. D. Kushlan, and Rundles, Pollard, Rumball and many others. Then, one must also refer to the cases of gastrostaxis discussed by W. Hale White and Carlos A. Pons, of Asbury Park, and others. Recently, there was the case of a well-known Philadelphia orthopedic surgeon, who for many years suffered from intractable duodenal ulcer, and hemorrhages, and underwent several operations. While in Maine, he suddenly developed massive gastric hemorrhages. When operated upon, nearly total gastrectomy was performed by Dr. Isidor S. Ravdin. The hemorrhage came from a large hemangioma.

Hodgkin's disease involving the stomach, may give rise to massive hemorrhage. Finally, severe gastrointestinal hemorrhage has been observed, in "healed or arrested ulcer" patients, who have received anticoagulant therapy tromexan, heparin, and dicoumarol, for other conditions coronary thrombosis, thrombophlebitic complications, polycythemia vera, pulmonary infarction, and multiple embolization. In such tragic and catastrophic episodes, one must be prompt in administering intravenously protamine solution, toluene-blue, and whole fresh blood transfusions! We have travelled far since Hippocrates discussed "atrabilis" —gastric hemorrhage, etc., and who gave us the term "carcinoma" or "cancer"! We have all met with severe hemorrhages in cases of advanced portal hypertension, cirrhosis of the liver, gastric and esophageal varices, Banti's syndrome, and thrombophlebitic spleen! These conditions may sometimes, also, occur in some of our long-standing ulcer patients!

Warren E. Coggeshall and Pasquale D. Genovese, of Indianapolis, reported on rupture of an abdominal aneurysm associated with massive gastrointestinal hemorrhage and referred to Rottino's collection of 31 cases of rupture of an abdominal aneurysm into the gastrointestinal tract, and Hunt and Weller collected additional nine cases including their own case. The report of Coggeshall and Genovese includes eight cases which they collected from the literature—making a total of 49 cases.

The late Donald C. Balfour, of the Mayo Clinic, gave, as "The Mary Scott Newbold Lecture", December 6, 1922, before the College of Physicians of Philadelphia, a discourse on *"Hematemesis"*.

Finally, B. Steinmann reported severe ulcer complications and hemorrhages, induced by sympathectomy and splanchnicectomy.

According to Mikal and Campbell of Boston, in their series of cases of carcinoma of the pancreas,—20 per cent of the patients with pancreatic carcinoma had gastroduodenal ulcerations from tumor invasion which simulated peptic ulcer with massive upper gastrointestinal hemorrhage.

Dr. Earl J. Halligan (Jersey City, N. J.):—I was very much honored to have Dr. Bancroft discuss our paper because he has had a vast experience in these things, and I know his judgment is good, sound and sensible, and that is what we need in the treatment of these particular cases.

We considered the buffer solution, and I am very glad that Dr. Bancroft has had two experiences with this, but I think possibly we became a little prejudiced because of Evart Graham's analysis. He said very tersely in the report that came from Detroit (B. M. Daly), that any method that gave a 20 per cent failure was interesting but not impressive. Consequently we didn't use it, so we have had no experience with it. Later reports are better but are probably not applicable to the type of case that we are discussing under our indications. However, one should give it a fair trial to evaluate it properly. I am glad that two cases recovered under that treatment.

The problem of potassium has been a difficult one. We have had on order a flame photometer in order to determine potassium levels. We have been trying to determine them by electrocardiographic readings, a lowering of the T-wave, a prolongation of the QRST-wave, but they have to be in pretty bad shape before we know that they have a deficiency of potassium, so we have been depending on clinical appearance. We hope to do better with potassium after we get the flame photometer.

The veins are often well used up with multiple transfusions, but there are two methods we must not forget, administration of blood by sternal or tibial puncture, the other is by giving it through the femoral vein. We have been desperate at times and have used the femoral vein for transfusion. It is not so difficult or so dangerous if you remember the anatomy, and it is not too hard when you are stuck. We have even used the external jugular vein when necessary.

As to the esophageal varices, that is really a problem. We have been very much interested in the esophageal varices, as Dr. Bancroft has said. We have been toying with the idea of using Garlock's method of packing the mediastinum through an incision in the neck parallel to the left sternomastoid muscle in order to do at least two things, not only to stop the acute hemorrhage but also to cause enough granulation tissue and fibrosis to eliminate the varicose veins and then, if it does recur, go in through the right side, that is, do right-side thoracotomy, expose the esophagus, after incising the mediastinal pleura and pack around it with gauze strip all the way down in order to have the same thing on the other side. I don't know how valuable that procedure is. It might work.

Dr. Perkel has had one little girl with massive hemorrhage from esophageal varices, but the Paton tube controlled that—and it wasn't really a Paton tube; it was apparently the Blakemore modification of the Paton tube.

Dr. Goldstein spoke about bleeding from other causes. We recognize bleeding from many other causes. One reads about Goldstein's disease, hereditary telangiectasis. The diagnosis was evident in our case because we saw the telangiectases all over the body, in the mouth, and so forth. We didn't try to operate on that case because it would have been of no avail. While we might correct the local condition, the bleeding might have started all over again some place else. Our report has been confined to the usefulness of surgery in massive hemorrhage from stomach and upper intestine.

In conclusion, I thank the discussers very much, because I really depended upon Dr. Bancroft's enlarging upon this subject as he has. We have used his operation, (not for duodenal ulcer with massive hemorrhage) which is very valuable, when we could not remove the duodenum because of either one of two things; that is, the poor condition of the patient, or because we could not close the stump safely. However, lately we have adopted another procedure, where the closure of the stump might not hold, and we can also use it under the same circumstances in bleeding ulcer, and that is, instead of trying to close the duodenal stump—as long as you are sure you have isolated or removed the ulcer and controlled the bleeding, you can—(well, I didn't mention it because I thought it was technical and since this is a gastroenterological society, I didn't discuss the technic) use another method in doing subtotal gastrectomy. After cutting across the duodenum, instead of completely closing the duodenal stump we insert a mushroom catheter into the duodenum, close the duodenum around it with a purse-string suture, the subtotal gastrectomy is completed, then a jejunostomy is done. The tubes from the duodenum and jejunum are brought out through separate stab wounds in the abdominal wall and connected with a glass tube. We have control of hemorrhage and, in addition, do not get the bad effects of the duodenal fistula often so disastrous when it occurs due to blow-out of the duodenal stump.

We have had several cases of leakage but fortunately had inserted drains so although recovery was delayed, the result was not tragic. Our primary purpose in using this method was to avoid leakage where proper closure of the duodenal stump could not be done. The tubes are removed in twelve to fourteen days. They heal up in twenty-four to forty-eight hours, and they have a beautiful recovery.

REMARKS ABOUT ULCER AND ULCERIFORM CANCER OF THE STOMACH

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I had the opportunity of recently reading many American works about ulcer, and I was astonished to see how much those opinions differ from what is thought here by many of us. So I beg my American colleagues to let me tell how experience has led me to consider some questions concerning ulcer and also the ulcer-simulating cancer.

Ulcer, in its typical forms, behaves like a local allergic manifestation, which spontaneously appears and disappears after three or four weeks, and which later appears, generally in the same place. From that, one can deduce that the height of gastric chlorhydria upon which so many authors still insist, has absolutely no practical importance in the pathogeny. If a lesion may heal in a hyperchlorhydric medium, it means that medium has no action on its production. The pathogenic problem is not only as to how it arises, (which is always considered), but how it spontaneously cicatrizes.

In practice, the measure of gastric chlorhydria is not important for diagnosis. Many cases of gastritis, and nearly all of our cases of small ulceriform cancers, are accompanied by an increase of acidity. Hypochlorhydria and achlorhydria are the results of extensive cancers.

The theory of gastritis, considered as the natal ground of ulcer, is no less false. German authors, and especially Konjetzny, have admitted that the banal gastritis becomes erosive gastritis, and that erosion transforms itself into ulcer. This would be a very simple opinion if it were true. In reality, between erosion and ulcer, there exists an anatomic difference, a difference not of degree but of nature, and one can scarcely see an erosion transform itself into an ulcer. Let us say, in addition, that when gastritis exists in an ulcer case, its seat may be very far from the ulcer, and the fairest types of gastritis are seen in duodenal ulcer.

Gastritis and ulcer are two different manifestations, but they are both very frequent, and it is not astonishing to see their coexistence.

If gastritis does not lead to ulcer, on the other hand, ulcer may produce gastritis, by stenosis, by neighboring irritation, etc.

It is important to know in each case if those two different lesions are associated or not, for gastritis requires a different treatment than ulcer. I shall simply say, that gastritis manifests itself with "burnings" and ulcer with "cramps"; that in gastritis certain substances (wine, and especially white wine, sugar and especially cooked sugar like jams, alcohol, aspirin, etc.) produces immediate—or sometimes late—burnings, which never occurs in ulcer in which late cramps are regularly pro-

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duced every day, by all foods, when the disease is in a period of activity. Radiology and gastroscopy may also help to determine if there is or is not an associated gastritis.

About medical treatment of ulcer, I have read many things in reviews; but I never see mentioned the methods which seem to me the most useful.

In order to rapidly alleviate the ulcerous pains, I prescribe daily intravenous injections of an ampule containing one milligram of neutral sulfate of atropin with one gram of bromide sodium in 10 c.c. of distilled water; or intravenous injections of ½ mg. of neutral sulfate of atropin and 2 or 3 c.c. of novocain at 1 per 100. Those injections very rapidly relieve the pains, but are only antalgic. It is necessary to add to them, or to begin after them, the real effective treatment of the disease. For that, nothing seems to me more efficient than intravenous injections of proteins.

Before the war, I used "Soluprotin-Roche," but this product can no longer be obtained. I have replaced it with intravenous injections, one every two days, of "Staprolysat III (a microbian protein) ½ c.c. progressively to 2 c.c. and sometimes, if well tolerated, to 2½ c.c. or even 3 c.c.; the doses are diluted in 10 c.c. of hyposulfene.

I use also a purified, fatless, milk-protein, Lactoclase, with 10 c.c. of hyposulfene; of that mixture, I prescribe progressively 1 c.c. to 5 or even 10 c.c. intravenously, one injection every two days.

The patient absorbs, immediately after the injection and a quarter of an hour later, a tablet of sanedrine, as antishock. But both methods are rather mild, and it is not necessary to obtain general reactions. On the contrary, if this happens, it is recommended to return to a smaller dose.

The treatment consist of 30 injections, given slowly, one hour or more before meals.

Those products give me better results than all the others I have tried, including injections of pepsin and of different hormones and also of other substances which appear from time to time on the gastroenterologic horizon, and then disappear.

When this first intravenous attack-treatment is completed, it is absolutely necessary to continue a treatment. I prescribe every month 12 subcutaneous or intramuscular injections of Laristine with Vitamin C.

Naturally, during the whole treatment, the patient takes bismuth, or aluminum hydroxide, or another similar powder. He takes it one hour before eating. But I have a long time ago renounced the Sippy-method, tedious for the patient and thoroughly useless.

This leads us to talk about diet.

The diet, for the ulcerous patient, has absolutely no importance. I have seen patients who drank only milk for years and who had two or three ulcerous periods yearly. I have also seen others (but I do not report it as an example to be followed!) who drank hard, ate very salted, peppered and spiced meals, and had

nevertheless only one painful period every two or three years and between those periods, they never suffered.

For the clinically nongastritic ulcerous patient, the ideal is a normal, well-chewed diet, avoiding over-spiced food and too greasy meals which remain longer in the stomach. This diet includes raw elements (ripe fruits, grated carrots, etc.). If they are not tolerated, I add medicinal vitamins, (although I am not a vitaminomaniac).

Therefore, I have abandoned all the "specialized" diets, not only the fastidious Sippy-diet, but also all others, Smithies, Coleman, Jarotsky, etc., with their useless chronologic and standardized progression, and also, of course, the new-born and distasteful protein hydrolysate diet. I repeat there is no practical advantage in all those strict-observance diets in comparison with the ordinary, reasonable, well-chewed one.

As for the milk-diet, I reserve it for the patients who suffer with a very violent attack and who tolerate nothing else; I never continue it more than a few days.

But there are patients, who are clinically gastritic, i.e. who have burnings when they eat special foods. For those patients, of course I give a more strict diet, according to their own tolerance. For them, also, a special treatment is indicated, mixed with the ulcerous one, for instance collargol at 3 per cent in a tablespoon of water, half an hour before meals, etc.

I daily see 20 to 30 ulcers at the hospital and in my private practice. I advise five or ten of them to stay in bed. I consider it is absolutely useless and unjustified to have the ulcerous patients treated in bed or in a clinic. The immense majority are as well cured with a simple, ambulatory treatment, allowing them to continue their normal life, as with strict milk-diet, bed, clinic, and all complicated methods I see praised every day. And if relapses may later occur, they occur as well in patients who have had one or two months of bed and milk as in the others.

Tobacco acts especially as a stimulant of the gastric secretion. It is absolutely indifferent to excite this secretion in a moment in which it is physiologically excited, I mean during the digestion. So I allow my ulcerous patients the use of tobacco but I forbid them to smoke when their stomach is empty (with the French hours, about two hours before eating).

I advise always to have the teeth examined if necessary with x-rays, and also the tonsils, because I think, agreeing this time with the American authors, that in some cases—more often in gastritis or in duodenitis than in ulcers—focal infection plays an important part in the production of gastric lesions. But I insist upon the words "some cases"; and I cannot disapprove enough the systematic removing of teeth, tonsils, appendix, etc., finally leaving only the patient—with his ulcer.

Of course, advice of calm, happy and carefree life is always useful. But it is not easy for all patients to follow them, even if the old-known reactions of the nervous system upon the organs are called "psychosomatic".

One of the things which surprises me more is the repeated mention that it is necessary to operate quickly in gastric ulcer "because it is impossible to diagnose

between a malignant and a benign lesion". This problem appears to me however in general to be very easy.

To resolve it, the clinic is of no value. Nearly all ulceriform cancers* simulate ulcer more or less—often more—with its late pains, its periods, its spontaneous and sometimes its therapeutic improvements, its hyperchlorhydria, etc.

Gastroscopy, in spite of the many articles and books written by the most eminent gastroscopists, has not yet resolved the question, and it needs, to give them results in the early diagnosis of cancer, much science, much faith and much imagination.

I agree with all that has been written about gastroscopy in gastritis, with the greatest part of that which has been published about ulcer, but with very little indeed about cancer. It is always luck when a very small cancer, what I really call "cancer incipiens", is detected with gastroscopy. I have led the surgeon to the operation on many cancers of the stomach which could not be seen or felt, and some of them were invisible after the operation when the resected stomach was opened; only the microscope showed a typical cancer, limited to the mucosa.

For the diagnosis of the nature of larger cancers, still "incipiens", the differences of coloration are of little value. On the resected stomach, it is impossible to distinguish accurately a benign and a malignant lesion. There are ulcers which begin to transform themselves, and also incipient cancers, which are identical in shape and color with a banal ulcer. The usual gastroscopic descriptions concern more extended cancers; in those also it may fail, and I have a lot of monstrous errors made by the most competent gastroscopist. So I consider that in the diagnosis of incipient cancer, gastroscopy has its place, which is, till now, small. Only the radiologic evolution is accurate and we shall see it in the diagnosis.

So, I cannot agree with the idea that "radiologic findings are not often conclusive," especially when one speaks of the most common places of cancer, the lesser curvature; but the radiographs must be well done and well interpreted.

They must not now be "too good". I have observed traveling in Europe and in South America, that the technic, wanting to be "modern", is wrong. All our incipient cancers were found on serials taken on barium-filled stomachs, on patients in procubitus, sometimes helping with pharmaco-radiology, never with compression. So I consider that radiographs in which one seeks to see the rugae of the mucosa, taken with compression, with tachygraphs, on only half-filled stomachs and on standing patients, are the best means not to see a "cancer incipiens". Those methods allow examining 30 or 40 patients in one hour, but examining them badly.

When with a correct method, little radiographic signs are detected, and interpreted by people who know what the signs of "cancer incipiens" are, one must not consider them as a sure diagnosis, before having studied their therapeutic evolution.

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*The terms generally used are amphibiologic. "Malignant ulcer", "ulcero-cancer", "ulkuscarzino", etc., may mean as well a cancer grafted on a real ulcer as a primitive cancer which has the appearance of an ulcer. I have proposed the following terminology which is adopted in several countries of Europe: "Ulcère transformé" for the benign ulcer which becomes malignant, and "Cancer ulcériforme" for the primitive cancer whose macroscopical appearance is an ulcer one.

Radiology hitherto, helped with therapeutic proof, (what I have called "radio-therapeutic test") seems to me the only effective mean.

I have described several radiologic aspects which one must consider as "suspect": the "niche en plateau" the "niche encastrée", and many other aspects of ulceriform and of infiltrated cancer. Knowing these descriptions, it is impossible to let pass as banal an abnormal appearance of the lesser curvature, as small as it may be. I cannot here go into greater detail. Those who are interested in the subject may read my books and look at their illustrations.

When one of those aspects is recognized, an intravenous protein-therapeutic treatment is effected during about one month and a half, and new radiographs are made. The films are compared with the first ones.

a) The niche in the benign ulcer disappears, or at least diminishes considerably.

b) If it only slightly diminished, one must make a differentiation (which is of extreme importance in gastric pathology) between the vertical and the horizontal part of the lesser curvature (the horizontal part including the angle).

In the vertical part, ulcers never become cancerous, but ulceriform cancer exists, though not as frequently as in other parts.

In the horizontal part, ulcer frequently becomes secondarily cancerous, and ulceriform cancer is frequent.

On the vertical portion, one is therefore authorized to again institute treatment, then new x-rays, and then judge.

On the horizontal part, it depends on many circumstances, which I cannot elaborate here,* but in principle, it is better to operate.

c) If, with the treatment, the niche remains unchanged, still more so, of course, if it increases, one must operate, even if the patient seems clinically cured; in fact, when under the treatment, the pains disappear and, at the same time, the niche increases, cancer is certain.

Resuming very schematically, it is possible to have a general view on the question with the following rules:

Certainly benign lesion:—Spontaneous or nearly spontaneous disappearance of clinical and radiologic signs after an ulcerous period.

Disappearance of clinical and radiologic signs after an active treatment (type of intravenous protein therapy).

Probable benign lesion:—Disappearance of the clinical signs after treatment; diminution of radiologic signs.

In practice, clinical recovery with only radiologic diminution is a favorable sign; it does not justify either the stopping of the treatment nor the cessation of the control.

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*I cannot discuss details here. For instance there are cancerous niches which do not represent an ulceration, but a denivellation in an infiltrated zone. In these cases, the extending of the cancer may lead to the disappearance of the niche but the stiffness increases and allows the diagnosis.

May the reader consider that I sum up here thousands of pages I have written on those subjects.

Very suspect lesion:—Persistence of clinical and radiologic signs.

Practically certain cancer:—Persistence of clinical signs and increasing of radiologic signs.

Certain cancer:—Clinical healing and progressively increasing of radiologic signs.

(This shows the absolute necessity of radiologic control in gastric "ulcus", even if the patient seems clinically cured.)

This method can only lead to one error of diagnosis: to operate what is thought a "cancer" and to find, in fact, histologically an ulcer; but as this ulcer had not been cured, it is a harmless error.

In any case, it avoids the irremediable and impardonable error: to bring a cancer, by long months medical treatment, to the phase of inoperability.

The objection made, that this practice leads to waste of time, is not valid. Cancer at the beginning grows very slowly, contrary to what is written by the classic authors, who did not know these incipient forms; they grow more slowly than the time needed for the diagnosis. Only in more extended cancers, time has an urgent value.

So, I think this way is the only one, till now, which allows systematically the early diagnosis of the cancer of the stomach. All other forms are uncertain or false. I allude for instance to the always-repeated axiom that "niches of more than 3 cm. are always malignant". Let us only say that niches of the size of a tangerine or of an orange are nearly always benign on the vertical part, and these "giant ulcers" are very easily cured in one or two months. On the contrary, all incipient cancers I have seen on the horizontal part (and sometimes on the vertical) had of course very small niches. This "axiom" should be erased.

So it is also false that "a short history means cancer and a long history means ulcer"; but it would be too long to expand this point here.

I cannot examine in detail the other localizations. For instance, it is said that niches of the greater curvature are all malignant. Generally the ulcers of the vertical part of this curvature are benign and those of the horizontal part, malignant.

I finally ask the reader to excuse me if I too often make reference to my own work. But I am obliged to: the "Cancer de l'estomac au début" is the only book concerning this subject in the world. But it is written in French, so it can be read only in Europe and in South America.

I can say that my assistants, my friend Dr. Albot and myself, have led to the operation of about 300 cases of incipient cancer. In most of those, cancer touched only the mucosa; in the more advanced cases, the submucosa was slightly invaded, but the muscularis mucosa was still untouched. The lymphatics were involved. We have of course a greater number of "small cancers", but none "incipient".

All our patients who had incipient cancer and were operated before the war are living and cured (except two, who died at 70 and 75 years with uremia or cerebral hemorrhage). The oldest case was operated 13 years ago[1].

So I consider that, when the patient consults us in time, the problem of the early diagnosis of the cancer of the stomach (especially on the lesser curvature) is now resolved. I am sure that more early methods will be found one day (serum, reactions, selective substance, application of Papanicolaou's principles, etc.). For the moment, we shall continue with the method I have described.

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1). Our patients operated on for the same conditions after the war are well also; but the time is too short to make a definite conclusion.

The cases I speak of are mucus-limited cancers, the submucosa or the muscularis mucosa being uninvaded. We have also cases of "cancer in situ", using the international terminology.

All our histologic preparations may be examined by those who ask it.

CHAPTER ACTIVITIES

Boston Chapter

A meeting of the Boston Chapter of the National Gastroenterological Association was held at the United States Marine Hospital, Brighton, Mass. on 29 March 1951.

Dr. Henry Baker, President, presided.

Following a dinner served by the hospital a scientific program was presented.

Cleveland Chapter

An organization meeting of the Cleveland Chapter was held at the Oakwood Country Club in Cleveland, Ohio on Tuesday evening 1 May 1951.

Those present were the dinner guests of Dr. Samuel Berger who was selected as temporary chairman of the Chapter.

The meeting was attended by approximately 15 physicians from the Cleveland area as well as by Dr. Roy Upham, Secretary-General and Mr. Daniel Weiss, Executive Officer.

Dr. August L. Chinn was selected as temporary secretary of the newly formed Chapter.

Grand Rapids Chapter

A meeting of the Grand Rapids Chapter of the National Gastroenterological Association was held at the Ferguson-Droste-Ferguson Clinic and Hospital, Grand Rapids, Mich., on Monday evening, 30 April 1951.

The host at dinner was Dr. Lynn A. Ferguson and the meeting was attended by over 70 physicians including all members of the Chapter.

Dr. Roy Upham, Secretary-General spoke on "Diarrhea" at the scientific session of the program.

Los Angeles Chapter

The Los Angeles Chapter of the National Gastroenterological Association held a meeting on 15 March 1951 attended by several members of the Chapter as well as members of the San Francisco and Santa Barbara Chapters.

The guest speaker of the evening was Dr. William W. Lermann, President-elect of the National Gastroenterological Association, who spoke on "The Gastrointestinal Tract as the Greatest Focus of Infection in the Human Body".

New Jersey Chapter

A meeting of the New Jersey Chapter of the National Gastroenterological Association was held on 24 April 1951 at the Academy of Medicine of Northern New Jersey.

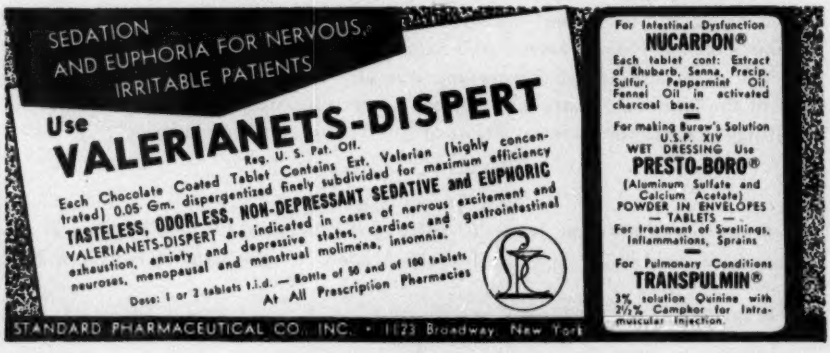
Following a routine business meeting a scientific program was presented.

New York Chapter

The annual meeting of the New York Chapter of the National Gastroenterological Association was held at the home of Dr. Samuel Weiss, New York City on 23 May 1951.

The following officers were elected for the year 1951-52: Dr. I. Ritter, President; Dr. Harry Barowsky, 1st Vice-President; Dr. Frederic W. Bancroft, 2nd Vice-President; Dr. A. X. Rossien, Secretary; Dr. Elihu Katz, Treasurer; and Dr. Milton J. Matzner, Recording Secretary.

Dr. William C. Jacobson is the retiring president.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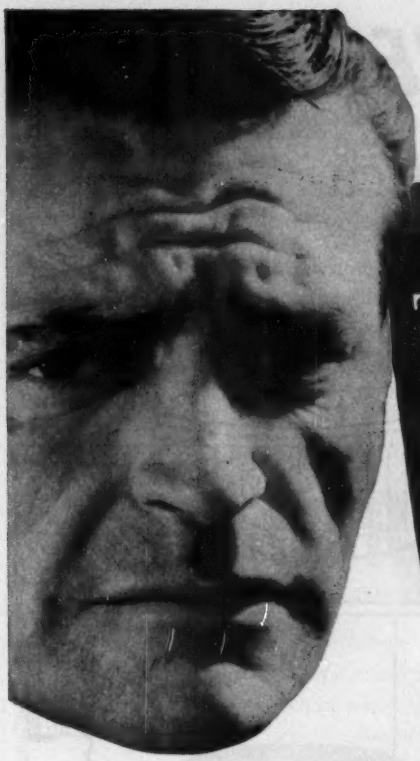

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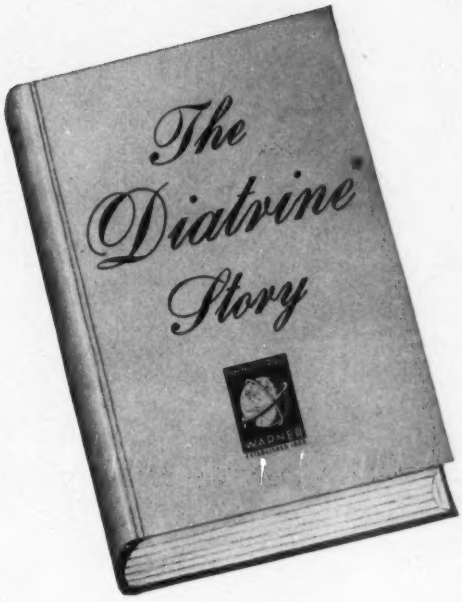

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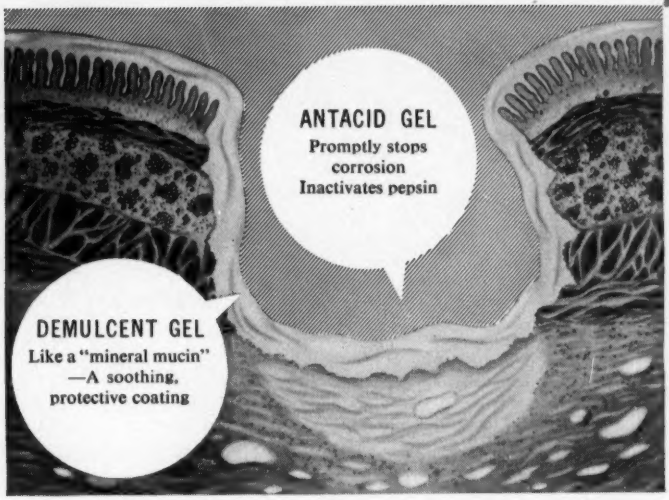

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